NEW GUINEA PATHOLOGY

A MORPHOLOGICAL STUDY OF HUMAN DISEASE

in the

TERRITORY OF PAPUA AND NEW GUINEA

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FOREWORD

Medical men who accompanied the administrators and traders of the sea-faring nations of Europe into the tropical regions of Asia, Africa and America were confronted with a bewildering array of diseases. The body of knowledge accumulated as a result of their observations came to be known as Tropical Medicine. Most textbooks devoted to this subject which were published prior to 1950 consisted almost entirely in descriptions of parasitic and other infectious diseases. Since then greater emphasis has been placed on the marked differences in all types of diseases - neoplastic, degenerative, environmental and genetic, as well as infective and parasitic, that exist between tropical and non-tropical countries.

This thesis consists in a morphological study of human disease in the Territory of Papua and New Guinea* - until recently one of the least known countries of the tropical world. During the 1960's a number of investigations were undertaken, both by the Department of Public Health and by many individual workers, to define the types of diseases prevailing during that decade; and in particular, to identify diseases which occurred nowhere else in the world. It was recognised that the information which came from these studies would be important for the health administrators, teachers and research workers who would be concerned with the immediate future. But in view of the ambitious and far-reaching plans for the development of the country, it will also be useful as a baseline for comparison in future decades when the population will have been exposed to drastic socio-economic change. In this thesis, the data from these various sources will be

* Henceforth called T.P.N.G.

analysed in conjunction with that accumulated by the author, who was the first pathologist able to examine material from all parts of the Territory.

ABSTRACT

A wide range of topics was investigated. The most important observation was that amyloidosis, especially primary amyloidosis, was more prevalent than in any previously studied population. No genetic or familial factors were recognised, and no specific cause was found to explain the unique prevalence of this condition. It occurred with equal prevalence throughout the country, and resembled the amyloid found in other countries. The majority of the patients presented to hospital with signs and symptoms of renal disease. A number presented with a goitre which was found to be due to amyloid infiltration of the gland. A combination of goitre and renal disease in children appeared to form a unique clinical syndrome.

Amyloid was found to be the cause of chronic renal disease in the majority of post mortems on such patients. Clinical observations in the Port Moresby General Hospital showed a similar, very high prevalence of amyloidosis, and a normotensive patient with chronic renal disease was likely to be suffering from amyloidosis.

Oral cancer accounted for 15.8% of the malignant neoplasms. It occurred predominantly in the coastal people, among whom the habit of chewing betel nut was almost universal. 10% of 315 cases of oral cancer studied personally were of the verrucous variety. These tumours occurred particularly on the labial commissures, on the buccal mucosa, or on both. This relatively high prevalence and this particular anatomical distribution were different from that seen in other countries.

Skin cancers were common. The lower leg was the commonest

site for squamous carcinomas. Melanomas occurred particularly on the feet and they appeared to be more prevalent in the Western and Southern Highlands than in any other area of T.P.N.G. An unusual feature was that 12% of 75 cases reviewed presented for treatment because of involvement of a digit, either finger or toe. Basal cell carcinomas were rare.

A tumour with clinico-pathological features identical to that of Burkitt's Lymphoma was encountered. It was not as prevalent as in central Africa, but T.P.N.G. was the only other country in the world where it occurred with anything like the prevalence seen in Africa.

Hepatoma and cirrhosis of the liver were common and the features of these two conditions resembled those seen in other countries in which the prevalence was similar. Jaw tumours, particularly ameloblastomas, were quite prevalent as in other tropical countries. Retinoblastomas were relatively common. Carcinoma of the cervix was common, while hydatidiform moles and chorionepitheliomas appeared to be more prevalent than in Australia, but not as prevalent as among the Chinese.

Infectious diseases were common; and well recognised conditions such as malaria, leprosy, tuberculosis, filariasis, donovanosis, yaws, mycobacterial skin ulceration, rhinoscleroma, scrub typhus and superficial mycoses all occurred, but there were no features specifically related to their occurrence in T.P.N.G. On the other hand, cutaneous amoebiasis affecting the ano-genital region appeared to be more prevalent than in other tropical countries.

Emphysema appeared to be as prevalent in post mortem lungs as it was in London, but relatively small amounts of carbon were present in the lungs in T.P.N.G. Cor pulmonale was the commonest form of heart disease encountered in clinical practice and this was most commonly a result of chronic lung disease, particularly emphysema. Myocardial infarction and cerebro-vascular accidents were rare.

A form of arteritis resembling Takayasu's arteritis of the aorta and its major branches, was encountered, and the clinico-pathological features of a group of these cases were described.

50% of 76 goitres removed surgically contained discrete, homogeneous, soft, creamy nodules. On histological examination these could easily be confused with malignant goitres, but it was postulated that they represented a response to severe iodine deficiency.

Various complications of pregnancy were common but it was interesting that four cases of foetus-in-foetu were encountered.

Anaemia was prevalent. This was most commonly due to iron deficiency. Megaloblastic anaemia due to deficiency of folic acid was relatively common in pregnancy. Thalassaemia and haemolytic anaemia associated with gross splenomegaly were also encountered.

Miscellaneous conditions encountered included:- unusual inflammatory conditions of the small intestine - acute Enteritis Necroticans (Pig bel), and Phlegmonous Enteritis; a relatively large number of cases of Dubin Johnson Syndrome which came particularly from the Madang area; a group of cases of Tumoral Calcinosis - a condition relatively common in Africans.

A series of neonatal autopsies was reported. This revealed no features which were peculiar to T.P.N.G.

A series of forensic autopsies was reported. The causes of these unnatural deaths - accident, suicide and homicide - reflected the social and cultural conditions in T.P.N.G.

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STATEMENT ON SOURCES

This thesis was compiled entirely by the author and the data contained therein is the result of personal observations unless otherwise indicated in the text. The compilation of this data would have been impossible without the co-operation and assistance of all the Medical Officers employed throughout T.P.N.G. during the years 1962 to 1967, and the assistance of the Australian Consultants, Professor R.E.J. ten Seldam and Dr. V.J. McGovern in histopathology, and Professor W.R. Pitney in Haematology. Specialised investigations were also performed by a number of other people - electron microscopy, Dr. J. Kerr, Department of Pathology, University of Queensland, Brisbane; tissue culture, specialised serology and chromosome analysis, Drs. J. Pope and D. Wallace, Queensland Institute of Medical Research, Brisbane; serum protein and immunoglobulin estimations in relation to amyloidosis, Dr. J. Hobbs, Department of Chemical Pathology, Royal Postgraduate Medical School, London.

The author attempted to make the study of pathology in Papua-New Guinea a clinico-pathological one; hence, close collaboration with many clinicians was actively fostered. Most of the papers reporting the results of this work were consequently published under joint authorship. However, unless otherwise stated, the pathological observations and the hypotheses relating to the clinico-pathological associations and syndromes were original. For example, the author recognised the high prevalence of amyloidosis and identified the syndromes mentioned in the text. The investigation of renal disease was also initiated by the author. Dr. L. Champness assisted in the collection and analysis of the clinical data, tested the validity of

the clinico-pathological associations, and maintained a careful watch for possible cases of amyloidosis in the medical ward of the Port Moresby Hospital. The author received a few cases of amoebic balanitis from the Western Highlands and then arranged a field investigation with Dr. Rodrigue who was the medical officer in the region, and who had submitted two of the cases for diagnosis. Further clinical data was accumulated by the author from cases notified to him from various parts of the country during the succeeding years. The presence of aortitis was observed by the author, and further data about the condition was accumulated as doctors throughout the country notified the author of other cases. A similar situation occurred in relation to the fourth case of foetus-in-foetu. The author diagnosed the first cases of Dubin Johnson syndrome on liver biopsies submitted for diagnosis. When a second biopsy came from the same area, the author notified the physicians in that area and suggested that other cases should be looked for. More cases were found and were further investigated, and the author was then able to bring together all the cases of congenital hyper-bilirubinaemia which had been diagnosed during the period under review. The data was then reviewed by the physician who had collected the largest group of cases.

The author was a member of the team which was investigating neoplastic disease in T.P.N.G. The tumour prevalences quoted were calculated in Dr. L. Atkinson's department in Sydney. Except where indicated in the text, the observations made on the clinico-pathological manifestations of individual tumours, for example oral cancer, jaw tumours, hepatomas, skin tumours, thyroid tumours and tumours of the female genital system, were made by the author. As indicated in the text, observations on other tumours were published

under the joint authorship of those involved in the investigations, and the author's part in the collection of the basic data on which these observations were made, is indicated in the text.

Those conditions which were studied personally are emphasised and treated in depth. In order that the whole subject might be seen in perspective, and so that it would be a more complete record of the disease patterns prevailing in the 1960's, mention has been made of relevant pathological conditions identified and described by others, with comments from personal experience. For the same reason, brief mention has also been made of conditions which occurred in T.P.N.G. but which did not have any specific features related to this fact alone.

Helpful suggestions were received from many colleagues, both in T.P.N.G. and in Australia, and the author is indebted to the technicians and clerical staff of the pathology departments in Port Moresby and at the Royal Brisbane Hospital for their assistance in the preparation of this thesis. Drs. J. Kerr and K. Hirschfeld very kindly criticised the manuscript.

R A Cooke

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CHAPTER 1

INTRODUCTION

The Territory of Papua and New Guinea comprises the eastern part of the island of New Guinea together with a number of off-shore island groups (Fig. 1). Running east-west along the mainland is a massive central cordillera composed of ranges with peaks rising to over 14,000 feet. The width of this mountain backbone varies from 50 to 150 miles; but in the wider section the ranges enclose broad, grass-covered valleys or intermontane plateaux having an altitude of roughly 5,000 feet. These elevated valleys flanked by high mountains are usually referred to as the Highlands and approximately half of the two million inhabitants of T.P.N.G. live here (Census of Papua and New Guinea, 1966). A Coastal plain to the North and another to the South of the central Highlands form two more distinct geographic regions. The off-shore islands, in particular the larger ones - New Britain, New Ireland, Manus and Bougainville may be regarded as another distinct region for the purposes of this investigation. (Fig. 1)

The people living along the North and South Coasts, and on the Islands have known Europeans since the late nineteenth century, but it was not until the 1930's that contact was made with the Highland dwellers. The people of T.P.N.G. belonged to a Stone Age culture which remained relatively unchanged for centuries until less than 100 years ago when they were first brought into collaborative contact with people from other countries. They lived in tribal groups which for the most part were hostile to each other. Travel within the country was further complicated by the extreme ruggedness of the

terrain, the presence of large rivers and swampy coastland, and the wide expanses of sea between the islands and mainland. The factor of isolation was accentuated by the existence of approximately 700 different language groups. The precise origins of the inhabitants are somewhat uncertain but there are obvious differences from region to region. The majority are Melanesians and have Negroid characteristics. Most of the rest are of Polynesian descent. A small group of Micronesians live on the North Coast.

Prior to the War in the Pacific, relatively little effort had been made to develop this area. Since the War however, progressively larger amounts of money have been allocated annually by the Commonwealth Government of Australia to the development of T.P.N.G. In 1946 for example the grant for T.P.N.G. was $4 million. By 1968 this had risen to $78 million. (Year Book of the Commonwealth of Australia, 1969). The efforts of Public Servants and private individuals who are assisting the native people to bridge the gap between Stone Age and the Twentieth Century (Fig. 2) are regularly appraised by representatives of the United Nations.

In common with many other developing countries, young people predominated. 38% of the people living in the Highlands and Coastal Regions were under 15 years of age, while in the Islands Region 45.3% of the inhabitants were in this age group. This can be compared with the situation obtaining in Australia in 1966, when 29% of the population were under 15 years of age. The youthful nature of the population of T.P.N.G. is due to a high birth rate, a recent reduction in infant and child mortality, and a high mortality rate in adult life. (Vines, 1970).

The Census of 1966 revealed a male to female ratio in the whole population of 1.09 : 1. In the larger towns, the male to female ratio was 2 : 1, due mainly to the movement of males to centres of employment. This fact alone contributed to the predominance of males in hospital patients - between 2 and 3 : 1 in most areas. Another factor which helped to account for this ratio was the inferior status of women. As in other primitive societies they were the labour force - providing food and firewood and looking after children - and they could not readily be spared to spend time in hospital. (Fig. 3)

Material and Methods

This review covers the six years 1962 to 1967. During this period all specimens for histopathological examination from all parts of the country were sent to the author's laboratory in Port Moresby. This included surgical specimens, and tissues which were removed during autopsies performed by doctors working in the different centres. During this period Professor R.E.J. ten Seldam of Perth, and Dr. V.J. McGovern of Sydney acted as consultants and advisers. In the two years 1964 to 65, the author was on study leave and the histopathology reporting was done by a series of locum pathologists. The records for those two years were examined, but only a limited amount of that data was used in the compilation of this thesis. When such data was used, the relevant histological sections were reviewed personally.

Surgical and post mortem specimens were photographed personally and many of the specimens were preserved and mounted to form the nucleus of a reference Pathology Museum for T.P.N.G. The author also took numerous clinical photographs so that clinico-pathological

correlations could be made. Further clinical photographs were taken by doctors throughout the country and many of these were loaned to the author on request for copying, at the time that histopathological reports were made.

Some of the data was analysed while the author was in T.P.N.G., but much of the analysis was carried out in the succeeding years. Some subjects were amplified by selected material which the pathologists in Port Moresby referred to the author from 1968 to 1970. The collection of clinical photographs was likewise expanded by copying some photographs kindly loaned by the following: Drs. L.T. Champness, C. Haszler, F.M. Cave, I.H. Buttfield and J. Kariks.

Virtually all the clinical and macroscopic pathology photographs were taken on kodachrome film, and negatives were made from these slides by Mr. B. Stewart, photographer, Department of Pathology, Royal Brisbane Hospital. All the prints for this thesis were made under his supervision, and those not actually made by him were made by the author, with a few being made by Mr. J. Silip of the Faculty of Medicine, University of Papua-New Guinea.

In order to investigate the clinico-pathological features of malignant neoplasms in T.P.N.G., a Tumour Registry was established in 1958 by Dr. L.T. Atkinson of Sydney, in co-operation with the Department of Public Health. Special forms were distributed, and medical officers throughout the country were asked to notify to this Registry any case of malignant neoplasm they encountered. Apart from epidemiological data the forms also included clinical descriptions of the neoplasms, and contributing doctors were encouraged to submit tumour tissue for histological examination.

A representative from the Department of Public Health was appointed Registrar to direct the Tumour Registry in Port Moresby. All the relevant data was transferred to punch cards, and duplicate cards were kept in Dr. Atkinson's Department of Radiotherapy in Sydney. This enabled statistical evaluations to be performed in Sydney, and was a safeguard in case one set of records was damaged.

From 1962 onwards any data received in the Histopathology Department relating to malignant neoplasms was referred to the Registrar. From that time there was a sharp increase in the number of cases notified annually, and the Registry functioned smoothly and efficiently.

Unless otherwise stated the tumour prevalences quoted were those found in the 3,085 tumours collected in the ten years 1958 to 1967.

Difficulties Encountered in Collection of Data

Conditions of Work

The conditions under which expatriate staff were working were a complete contrast to those to which they were previously accustomed. In general terms, qualities of adaptability, patience and perseverance were required to cope with the day to day problems.

Absence of Basic Data

Prior to 1962 there was a dearth of information about almost all aspects of the health and disease patterns of the population. Although pathologists had been stationed in Port Moresby, Rabaul and Lae both before and after World War II, their facilities were limited and they had access to only small amounts of morbid anatomical and

surgical pathological material. Virtually all that had been written about the pathology of the country was contained in three short articles by Backhouse (1955, 1956 and 1958). These were written 20 years after he had left the country. Dr. A.V.G. Price, pathologist in Port Moresby to 1962 was able to do only a small amount of histopathology, so these records were of limited value. The consultant pathologists were appointed a few years prior to 1962, but only a relatively small amount of material had been referred to them, because of the bother involved in dispatching formalin fixed tissue to Australia.

During the period in which this pathological data was being accumulated, numerous other investigations were being conducted to help elucidate patterns of health and disease which existed in the country. As indicated elsewhere, the results of many of these investigations have been published during the last three years.

Case Histories

Accurate case histories were not easy to obtain owing to language difficulties, and interrogations were frequently conducted in sign language. The people had little concept of time, which meant that the age of the patient and the duration of the symptoms could only be guessed at.

Communications

The majority of the doctors were working in areas far removed from Port Moresby, and all communications between them and the pathologist had to be made by letter. In the more remote areas the

mail service was rather precarious and mail deliveries were irregular and relatively infrequent. When insufficient clinical detail was given on the pathology request forms, there was often a long delay before further information could be obtained. Because of these difficulties, pathology reports to the remote areas were frequently delayed. In urgent cases some reports were made by telegram or by radio-telephone.

Follow-up

There was no written language, and names written in hospital records and on pathology request forms were the nearest phonetic sound that the medical officer thought the patient was making when asked to give his name. In many areas, particularly around Port Moresby, the people had more than one name and would not always give the same name at each admission to the hospital. In many such cases the only way of knowing whether the patient had been admitted before, was for him to be recognised by one of the medical staff. Since there was a rapid turnover of medical officers in most hospitals, this method also had its limitations.

A hospital record system was introduced into Port Moresby Hospital in 1960, but this was the only major hospital in the Territory in which case records were properly filed and indexed during the period under review. Particularly in the more primitive areas, patients would often not remain in hospital long enough for the results of special investigations such as histopathology tests to reach the doctor who was treating them. Alternatively they sometimes left hospital and returned to their homes before a full course of treatment could be completed. Having left the hospital they would return to

their village, which, even if marked on a map was likely to be relatively inaccessible, and the doctor himself was usually too busy to conduct follow-up studies under such circumstances.

Post Mortem Examinations

Approximately half of the post mortem material reviewed came from post mortems performed outside Port Moresby. These examinations were performed by medical officers who usually had had no specific training in this form of examination. Hence, a disappointingly large number of these specimens had to be omitted from the study either because the blocks taken from the organs were inadequate, or the clinical details given on the request form were inadequate. Almost all the medical officers had a greater work-load than would normally be expected for one person, and to organise an autopsy was often a major undertaking. During the period of this review proper mortuary facilities with refrigerators and a table with running water were available only in Port Moresby, Lae, Madang, Wewak and Rabaul. In all other centres including the entire Highlands region there was no refrigeration for bodies and no running water. Thus, outside these centres post mortems were performed under extremely difficult conditions.

In some areas, particularly around Port Moresby there was a great deal of resistance to post mortem examinations being performed. Permission for autopsy was always requested from the relatives before such an examination was performed. Almost invariably, at least a few relatives would accompany a patient in hospital. A crowd of wailing mourners usually waited outside the mortuary, and sometimes a hostile

crowd was ready to oppose any attempt to perform an autopsy. Occasionally in coronial cases a police guard for the pathologist was essential. (Figs. 4 & 5). Frequently in Port Moresby the autopsy could be performed only on condition that one or more members of the family were allowed to be present. Following the examination, a formal demonstration of the diseased organs was given to these and other interested relatives. In the Highlands Region in particular, the mortuary was often a room with open sides. The post mortem examination was conducted in the full view of all the relatives and other curious on-lookers who would quickly congregate for the spectacle. When permission was obtained for only a limited post mortem examination, a small incision was made, and as many organs as possible were sampled through this incision.

It was the accepted practice for the relatives to take patients home to die if they were incurably sick and it was obvious that medical treatment was of no avail. This humane and sensible practice was a further limiting factor in the performance of post mortem examinations.

Technical and Clerical Assistance

It would have been impossible for the Pathology Department to function without the dedicated efforts of a handful of expatriate technologists because the standard of technical and clerical assistance was very low, particularly in the earlier years. Technicians were recruited locally and trained on the job. A formal training scheme for laboratory technicians was instituted in 1963 and following this the standard of work steadily improved.

CHAPTER 2

AMYLOIDOSIS

Amyloidosis, a condition in which a hyalin, eosinophilic material is laid down in the interstitial tissues of the body, was first described by Rokitansky (1842). Later on it was realised that while most cases were associated with diseases such as tuberculosis, chronic osteomyelitis, leprosy and other forms of chronic sepsis, some appeared to be unrelated to any other disease. Reimann, Koucky and Eklund (1935) introduced the concept of secondary and primary forms of the disease depending on whether some other predisposing chronic disease was present as well. With the recognition by Andrade (1952) of a form of peripheral neuropathy occurring in some families in Portugal, the concept of heredo-familial amyloidosis was introduced. Since that time further clinico-pathological syndromes of heredo-familial amyloidosis have been reported - Familial Mediterranean Fever (Heller et al, 1958); Urticaria, Deafness and Nephropathy in a Derbyshire family in England (Muckle and Wells, 1962); Familial Cardiomyopathy (Frederiksen et al, 1962); Familial Cutaneous Amyloidosis (Isaak, 1960) and Familial Amyloid-producing Medullary Carcinoma of the Thyroid (Williams et al, 1966).

In a recent comprehensive review, Cohen (1967) pointed out that much effort has been spent in an attempt to classify amyloidosis according to the gross and microscopic distribution of the infiltrate, and according to its variable staining properties. These classifications have been bedevilled by the fact that there is a good deal of overlapping between the various forms. Examination of the chemical

structure and metabolic turnover of the amyloid fibrils which is currently being undertaken, may lead to a more fundamental and satisfying classification.

An extraordinarily high prevalence of non-familial amyloidosis was found in T.P.N.G. (Cooke and Champness, 1967); (Cooke and Champness, 1970), and what follows is an account of this.

Material

The material which formed the basis for this study consisted of the surgical pathological and post mortem specimens submitted to the Pathology Department, Port Moresby between 1962 and 1967. Post mortems rejected from the series were neonates up to one month of age, expatriates, those in which post mortem autolysis was too advanced for histological examination, and those in which only one or two organs were sampled for histology. 81 cases of death from accidental trauma in which full histological examination was performed, were also included in the post mortems from the South Coast.

A diagnosis of amyloidosis was made when the haematoxylin and eosin stained sections of the tissue suggested this, and when it was confirmed by the presence of a green birefringence when stained with congo red and examined under polarised light. The cases were classified as secondary if, either in the clinical or in the post mortem findings, there was evidence of one of the diseases well known to predispose to amyloidosis. Where no predisposing disease could be found, the cases were classified as being primary.

There were 1,100 post mortems; 80 cases of amyloidosis

were found among these. A further 17 cases were confirmed on histological examination of surgically removed material. Of these 97 cases, 47 were classified as primary and 50 as secondary. Because of their greater importance and interest in the overall knowledge of amyloidosis, the primary cases were studied in greater detail. 34 primary cases were chosen for detailed study because the clinico-pathological investigations were more exhaustive on these.

Results

Prevalence

The prevalence of amyloidosis in the post mortem series was found to be 7.3%. Primary cases accounted for 3.3%. (Table 1)

TABLE 1

Prevalence of Amyloidosis in Post Mortems 1962-67

	Total	South Coast	North Coast	High-lands	Islands
No. Post Mortems	1100	371	377	274	79
No. Primary Amyloid Cases	36 (3.3%)	15 (4.0%)	10 (2.7%)	9 (3.3%)	2 (2.5%)
No. Secondary Amyloid Cases	44	11	4	23	6

When the cases were divided according to the geographical region in which the post mortem was performed, there did not appear to be any difference in the prevalence of amyloidosis in the different regions. ($P = 0.32$). The large number of secondary cases from the

Highlands could be accounted for because of the special interest of the Highlands region leprologist. There were relatively few post mortems from the Islands region because a pathologist was working independently in Rabaul from 1964.

No two cases were found in the same family. When the primary cases were plotted on a map according to the home village of the patients, the result was a random distribution throughout the country with particular collections around the towns in which the main hospitals were situated. (Fig. 6).

The age and sex distribution is shown in Fig. 7. There did not appear to be any significant difference between the age and sex distribution of the primary and secondary cases. 17% of the combined group occurred before 20 years of age and 59% between 20 and 40 years. This contrasted with 35% and 48% for similar age groups in the post mortems in which no amyloid was present. The youngest patient in the group of primary amyloidosis was a male aged 6 years, and the youngest patient in the secondary group was a female aged 7 years who had tuberculosis. The overall ratio of males to females was 1.7:1 indicating that there was no particular sex predominance, as this was approximately the sex ratio of hospital admissions. "Department of Public Health Hospital Disease Statistics 1963-64" (1967).

Pathology

No particular difference was noted between the anatomical distribution of the amyloid in the primary and in the secondary cases, nor was any macroscopic or microscopic difference noted. The anatomical distribution of the amyloid in the primary cases is shown in Table 2.

TABLE 2

Anatomical Distribution of Primary Amyloid

	Number examined	Amyloid present	Amyloid in vessels	Amyloid in interstitial tissue also
Kidney	36	36	36	36
Liver	33	33	33	0
Spleen	24	24	24	2
Heart	22	20	20	16
Lung	20	7	7	5
Intestine	13	10	10	8
Thyroid	9	9	0	9
Pancreas	11	11	11	2
Adrenal	9	9	9	2
Lymph nodes	9	8	8	0
Ovary	3	3	3	0
Testis	3	3	3	0
Parathyroids	3	2	2	2
Brain	4	0	0	0
Pituitary	4	0	0	0
Tongue	3	2	2	2
Ulna nerve	2	0	0	0
Submandibular gland	2	1	1	1
Prostate	2	2	2	0
Bladder	1	1	1	0
Ureter	1	1	1	0

Kidneys were examined in all the post mortem cases of primary amyloidosis. The average weight of 24 of these was 125 gms. compared

with an average of 130 gms. for 38 kidneys from adult Papuans with no evidence of renal disease. The kidneys of 11 other cases were described as being macroscopically normal by the person doing the autopsy, while 8 others were regarded as being small and contracted. Kidneys were larger than normal in a few cases, but most commonly they were either of normal size and appearance (Figs. 8 & 9) or smaller than normal, with finely nodular capsular surfaces and a reduced cortical thickness (Fig. 10). It was very difficult to make a firm diagnosis of amyloidosis on the macroscopic appearances of the kidneys. One helpful sign was a blurring of the demarcation between cortex and medulla on the cut surface. Staining with iodine was sometimes helpful in the macroscopic diagnosis of the renal amyloid, but in none of the other organs could the amyloidosis be detected with any degree of certainty prior to histological examination.

Amyloid was present in the walls of small vessels in all the organs examined. This was almost exclusively in a peri-reticulin type of distribution. (Heller et al., 1964). In the kidneys, deposits of amyloid were present in vessels, glomeruli and interstitial tissues. These deposits were usually heavy. (Fig. 11). In the liver, on the other hand, amyloid was present only in the small vessels in the portal tracts. (Fig. 12). In the spleen, the penicillar arteries were involved. (Fig. 13). Interstitial deposits were very uncommon and when present, were confined to the lymphoid follicles which were then usually completely replaced by amyloid. (Fig. 14). Interstitial deposits in the myocardium were typically small and patchily distributed. Deposits in the alveolar walls of the lungs were likewise patchily distributed. The interstitial deposits in the intestine were present in the lamina propria or in submucosa or in both. These were heavy

in some cases. (Fig. 15). Amyloid in the thyroid was deposited between the follicles. In some cases, particularly those with an amyloid goitre, the deposits were very heavy. (Fig. 16). Interstitial deposits when present in the pancreas and adrenal were small and inconspicuous. In all cases, however, the vessel walls were heavily infiltrated. (Figs. 17 & 18). The parathyroids examined were enlarged, partly as a result of amyloid deposition, and partly as a result of the secondary hyperplasia due to the uraemia. Tongue enlargement was encountered in the patient with Multiple Myeloma (Fig. 19) but was not noted in any patient with primary amyloidosis and this was reflected in the very small amounts of amyloid found in tongues examined histologically. (Fig. 20).

Electron Microscopy

Electron microscopy was performed on tissue from the kidney of one patient, and from the thyroid of another. In both, fine fibrils showing a regular beading were demonstrated. (Fig. 21).

Chemical Analysis

The amyloid present in the thyroid of one patient was extracted and purified. This material retained the fibrillary appearance of amyloid on electron microscopy, and stained with congo red. Two bands appeared on ultra centrifugation, one large and one smaller. The physico-chemical properties of this substance are being further investigated (Anders, 1969).

Tissue Culture and Chromosome Pattern

Skin biopsy was performed on one patient and a line of fibroblasts was established in tissue culture. A chromosome pattern was performed on these cells and a normal karyotype was found. (Fig. 22). The tissue culture was stained with congo red, but no amyloid was demonstrated. Electron microscopic examination of these fibroblasts was undertaken. They contained numerous microfilaments in their cytoplasm, but in accordance with Comings and Okada (1970), these were interpreted as being normal components of the cells and not amyloid fibrils.

Relationship to Cold Agglutinins

Booth (1965) reported the high prevalence of cold agglutinins in the sera of the inhabitants of T.P.N.G. Tested at 20°C. the prevalence ranged from 10% of the population in Port Moresby to 80% in Rabaul. At the author's request Dr. Booth tested sera from 6 patients with amyloidosis for the presence of cold agglutinins. Cold agglutinins in a low titre were found in two of these when tested at 20°C. This was interpreted as being no different from the results expected for a randomly selected group of normal Papuans and New Guineans.

Clinical Features

The clinical data from 34 patients with primary amyloidosis are presented in Table 3.

TABLE 3

Clinical Data 34 Primary Amyloid Cases

Main Presenting Features:

Uraemia	17
Diarrhoea	4
Cardiac failure	4
Nephrotic syndrome	2
Steatorrhoea	2
Dead on arrival at hospital	1
Died after delivery of a hydatidiform mole	1
First diagnosed in operation specimens:	
Thyroidectomy	2
Prostatectomy	1
	34

Specific Clinical Features:

* The number in brackets is the number of cases in which the clinical feature or laboratory test was specifically noted in the case notes.

Duration of disease	(25)	*Average in weeks	8
Diarrhoea	(26)	Present	12
		Malabsorption	2
Blood pressure	(28)	< 140/80	26
		> 140/80	2
Heart size	(25)	Enlarged	10
Arrhythmia	(25)	Present	4
Dependent oedema	(25)	Present	11
Ascites	(25)	Present	6

Specific Clinical Features: (continued)

Respiratory System	(22)	Normal	18
		"Moist sounds"	4
Liver	(22)	Enlarged	7
Spleen	(27)	Enlarged (up to Hackett grade 2)	8
Lymph nodes	(28)	Normal	27
		Mild enlargement of cervical chain	
		? infection	1
Nervous System	(23)	Normal	23
Thyroid	(23)	Enlarged	7
Tongue	(17)	"Thickened" ? enlarged	1
Salivary glands	(11)	Normal	10
		Parotitis terminally	1

Ancillary Investigations:

Albuminuria	(27)	Present	26
Microurine	(18)	Nil significant	16
		25-30 red cells/HPF	1
		Infection terminally	1
Blood urea	(29)	< 80mg%	3
		80-150mg%	6
		150-250mg%	6
		> 250mg%	14
Serum Potassium	(16)	< 3.5mEq/1	3
		3.5-5.5 "	6
		> 5.5 "	7

Ancillary Investigations: (continued)

Chest Xray	(22)	Normal	16
		Pulmonary oedema	3
		Lower lobe opacities thought to be non tuberculous pneumonia	3
Haemoglobin	(26)	8-10gm%	13
		5-8 "	8
		< 5 "	5
White cell count	(22)	4,000-11,000/cmm	16
		> 11,000 "	5
		< 4,000 "	1
Differential count	(19)	Normal	11
		Neutrophilia	5
		Eosinophilia	3
Malarial parasites	(22)	Absent	20
		Gametocytes only	1
		Ring forms present	1
Bone marrow	(5)	Aspiration	4
		Post mortem section	1
		None showed any plasma cell abnormality.	
Mantoux test	(5)	Positive	2
Rectal biopsy	(8)	Positive	6

Uraemia was the commonest mode of presentation, while a significant number presented with diarrhoea or malabsorption syndrome. 4 presented with cardiac failure and 2 with nephrotic syndrome. In 5 patients the diagnosis was made either at autopsy or on histological examination of the surgical specimens. According to the histories given by the patients, the duration of the disease from time of first presentation at hospital, until death was rather short. The majority of patients were normotensive. Hepatomegaly and splenomegaly were no more prevalent than in the general population of this malarious country. The nervous system was not involved. The thyroid was enlarged, firm, smooth and rather hard to palpation in a significant number of patients. Macroglossia was not noted.

Ancillary investigations revealed the presence of uraemia, (usually gross) in the majority. All the patients tested were anaemic. (See Chapter 16) . Malarial parasites were not significantly related to the condition. Bone marrows showed no increase or abnormality in plasma cells. The serum protein estimations performed by electrophoresis on cellulose acetate on 10 cases showed a very low albumin with a relatively high gammaglobulin. Immunoelectrophoresis showed a raised IgM in the group. The results of serum protein analyses on four groups of indigenous people - normal Port Moresby residents, leprosy patients whose rectal biopsies were negative for amyloid, patients with non amyloid chronic renal disease and patients with primary amyloidosis are shown in Table 4.

TABLE 4

Serum Protein Values

	Total gm/100ml.	Alb.	Glob.	Gamma	Ig G mg/100ml	Ig A	Ig M
Laboratory Normal values (Caucasians)	7.24	3.12	4.12	1.89	600-1600	150-450	50-150
Normal Indigenous Residents of Port Moresby (10)	7.09	3.63	3.46	1.63	1480	431	135
Leprosy patients Amyloid negative (21)	7.78	3.5	4.27	2.28	1790	352	169
Chronic Renal Disease Not Amyloid (7)	5.98	2.65	3.33	1.42	1128	274	256
Primary Amyloid (10)	5.59	1.80	3.79	2.0	1482	283	579 (range 85-1150)

Rectal biopsy was positive in 6 out of 8 patients subsequently proven at autopsy to have amyloidosis and this was found to be the most convenient method of obtaining a tissue sample for histological examination. As the amyloid was present only in the small vessels of the lamina propria, it could easily be missed unless the biopsy was adequate, and congo red stained sections were examined.

Illustrative Cases from Port Moresby

Case 1 - In this case uraemia was the main presenting feature. A male patient, aged approximately 30 years, had been complaining of abdominal discomfort, malaise, weakness, anorexia, vomiting, diarrhoea and weight loss for about two weeks. He denied having had any previous illness. On examination, he was fully conscious, afebrile

and slightly dehydrated. His blood pressure was 90/50 mm Hg, and the only abnormality noted clinically was splenomegaly. (Hackett grade 2).

A number of investigations were carried out, with the following results:

Urine: specific gravity 1010; albumin content 2.7gm/100ml; microscopy, no abnormality detected; culture, no growth.

Chest X-ray film: lung fields clear; cardiac outline normal.

Blood urea content: 194mg/100ml, reducing to 93mg/100ml after rehydration.

Serum electrolyte contents (mEq/l.): sodium 146, potassium 4.9, chloride 100.

Haemoglobin value: 9.7gm/100ml; leucocytes, 4,500/mm.^{3}

Peripheral blood smear: normal white cell distribution.

Erythrocytes: normochromic, normocytic; no malarial parasites seen.

Serum protein content: 6.8gm/100ml (albumin 2.0, globulin 4.8); IgG, 1,600mg/100ml; IgA, 220mg/100ml; IgM, 700mg/100ml.

Liver function tests: serum bilirubin content, 2.8mg/100ml; SGOT content, 71 Sigma units; SGPT content, 43 Sigma units; serum alkaline phosphatase content, 13.5 King-Armstrong units.

Faecal fat excretion: 0.2gm in 24 hours.

Culture of faeces: no pathogens isolated.

Two days after admission he developed a right-sided lower lobe pneumonia (confirmed on chest X-ray examination), with a temperature of 38°C. He lapsed into coma and died seven days after his admission, in spite of antibiotic and supportive therapy.

Autopsy

At autopsy, the right lower lobe pneumonia was confirmed. The right kidney weighed 210gm and the left 180gm. Both had very heavy amyloid deposition in the glomeruli, in vessels of all sizes, and in the interstitial tissue. The other organs appeared normal macroscopically, but amyloid was present in the small vessels of the spleen and liver, in the interstitial tissue of the myocardium and in the lamina propria of the intestine, as well as in the small blood-vessels of these latter organs.

Case 2 - Steatorrhoea was the main presenting feature in this case. A man, aged about 25 years, had suffered from abdominal discomfort, anorexia, severe diarrhoea and weight loss for about four months. Recently he had experienced malaise and lassitude to such an extent that he had been unable to work. He had no past history of serious illness and had never before been admitted to hospital.

Examination of the patient revealed generalised wasting, mild abdominal distension and the right lobe of the thyroid was just palpable and felt firm and smooth. (Fig. 23). The liver and spleen were not enlarged. The tongue had a smooth surface, but was not enlarged. The blood pressure was 110/70mm Hg, and no other abnormality was found.

A number of investigations were carried out, with the following results:

Urine: no albuminuria; microscopy, no abnormality detected.

Chest X-ray film: lung fields clear; cardiac outline normal.

Haemoglobin value, 10gm/100ml; leucocytes, 8,700/mm.^{3}

Peripheral blood smear: normal leucocyte distribution; erythrocytes, normochromic, normocytic; no malarial parasites seen.

Liver function tests: serum bilirubin content, 3.5mg/100ml; serum alkaline phosphatase content, 17 King Armstrong units; SGOT content, 27 Sigma units; SGPT content, 22 Sigma units.

Serum electrolyte contents (mEq/1.): Sodium, 136; potassium, 3.6; chloride 90.

Serum Protein content: 4.7gm/100ml (albumin, 1.6; globulin, 3.1); IgG, 1,125mg/100ml; IgA, 135mg/100ml; IgM, 130mg/100ml.

Blood urea content: 25mg/100ml.

Culture of blood: no growth.

Serum agglutination tests (Widal and Weil-Felix): negative response.

Faeces: Hookworm ova present; culture, no pathogens grown.

Faecal fat excretion: more than 30gm in 24 hours.

Sigmoidoscopy: friable, haemorrhagic rectal mucosa; biopsy, amyloid present in the walls of the small vessels in the submucosa.

In spite of treatment with a high-protein, low-residue diet, fluid replacement, antibiotics, steroids and salazopyrin, the patient's condition gradually deteriorated, and he died 28 days after his admission to hospital. His terminal progress was complicated by an acute left-sided parotitis and an urticarial rash (possibly drug-induced).

Autopsy

Amyloid was present in the vessel walls and interstitial tissue of the lamina propria in all the pieces of the small and large intestine that were sampled. The state of the mucosal epithelium could not be assessed because of post mortem autolysis. The pancreas appeared to be normal apart from the presence of amyloid in the walls of the blood vessels. Amyloid was present in the vessel walls of the liver, spleen and myocardium. The kidneys weighed 120gms. each and were not severely involved by amyloid which was present in the walls of some of the glomerular capillaries and some of the larger vessels. The thyroid was heavily infiltrated with amyloid which had caused destruction and wide separation of the thyroid follicles.

Case 3 - The main presenting features in this case were uraemia and a goitre. A boy, aged six years, was admitted to hospital in coma. He had been quite well until three weeks previously when he began to develop lassitude, anorexia, vomiting, diarrhoea (sometimes with blood-stained faeces) and bleeding from the nose. Examination showed him to be a comatose child, with slightly puffy eyes, scrotal

oedema and a moderately enlarged thyroid, which felt smooth and hard. The blood pressure was 120/80mm Hg. Oliguria was present.

A number of investigations were carried out with the following results:

Cerebro-spinal fluid: normal pressure; normal microscopic appearances.

Chest X-ray film: bronchopneumonia, slightly enlarged heart.

Urine: gross albuminuria; microscopy, no abnormality detected; culture, no pathogens grown.

Haemoglobin value, 7.0gm/100ml.

Peripheral blood smear: neutrophil leucocytosis; normochromic, normocytic erythrocytes; no malarial parasites seen.

Blood urea content: 200mg/100ml, rising to 350mg/100ml.

Serum electrolyte contents (mEq/l.): sodium, 120; potassium 5.4; chloride, 90.

Culture of blood: no growth.

Antibiotics were given and fluids administered intravenously, but the child did not recover consciousness and died two weeks after his admission to hospital.

Autopsy

At autopsy, the pneumonia was confirmed. The kidneys each weighed 30 gm and had coarsely granular cortical surfaces. They

contained heavy deposits of amyloid in almost all glomeruli, in the vessels and in the interstitial tissue. All four parathyroids were enlarged, partly owing to amyloid deposition and partly owing to hyperplasia. Clear cells were the main parathyroid cell type present.

There was no evidence of renal osteodystrophy. The thyroid and submandibular glands contained heavy interstitial deposits of amyloid, and amyloid was present in the vessels of the adrenals, spleen, myocardium, testes, lymph nodes, ureters, pancreas, tongue, small and large intestine, oesophagus and lungs. There were also small amyloid deposits in the interstitial tissue of the lungs and intestines.

The brain, meninges, cerebellum, brain-stem and ulnar nerve were normal and contained no amyloid.

Primary Amyloidosis in Children

In the present series there were four patients under 13 years of age. All four presented with symptoms and signs of renal disease. In three, a goitre was noted and confirmed histologically. (Fig. 24). In the fourth case, presenting in 1962, permission was obtained for removal of one kidney only, after death, and no comment was made on the thyroid gland either in the clinical or in the post mortem notes.

The author obtained information on four other children with amyloidosis. Two of these were diagnosed prior to 1962 and two after 1967. The clinical histories and histological material from these cases was made available by Drs. L. Champness, K. Powell and W. Garner. Two of these presented for surgical treatment of amyloid goitres and both died a few months later of renal failure but no post mortem

examinations were performed. The other two presented with symptoms and signs of renal disease, and a goitre was noted during clinical examination. The presence of amyloidosis in both thyroid and kidney was confirmed in both of these.

Thus, of 8 children with primary amyloidosis, 7 were known to have renal disease and a goitre at the time of presenting for treatment. The presence of amyloid was confirmed histologically in both kidneys and thyroid in 5 of these.

Secondary Amyloidosis

The diseases which were complicated by amyloidosis are listed in Table 5.

TABLE 5

Diseases Associated with Secondary Amyloidosis

Leprosy	30
Tuberculosis	12
Chronic lung disease, ? type	5
Multiple myeloma	1
Ankylosing spondylitis	1
Carcinoma of mouth with chronic chest infection	1
	50

The patients with leprosy constituted 60% of all the lepers included in the post mortem series, and those with tuberculosis 9% of

all those with tuberculosis. Apart from the large number of leprosy cases from the Highlands (the reason for which has already been mentioned) the geographical distribution of secondary amyloidosis paralleled that of the primary, being found in all parts of the country.

Discussion

The amyloidosis found in T.P.N.G. was similar to that found in other parts of the world in its histological appearance in haematoxylin and eosin stained sections, in its histochemical staining with congo red, and in the electron microscopic appearance of the fibrils. The chemical composition of the amyloid also appeared to be similar to that found elsewhere. (Mandema et al, 1968).

The amyloidosis found in T.P.N.G. was different from that in other parts of the world in the following respects:-

1. Prevalence

The most striking difference was the extreme prevalence of the condition. In most parts of the world the prevalence is approximately 0.5% of all autopsies. In Japan it is a very uncommon disease, accounting for 0.1% of autopsies. In countries in which familial amyloidosis is common (Portugal and Israel) the prevalence approaches 3% of all autopsies (Cohen, 1967).

In T.P.N.G., however, amyloidosis was present in 7.3% of all autopsies. Because tuberculosis and leprosy were so common, a relatively high incidence of secondary amyloidosis could have been expected. However, at least half the cases encountered were primary. This prevalence has been well substantiated. It was first noted by the author

in 1962-63. Review of the material collected in the Department of Pathology during the author's absence in 1964-65 showed a similar figure, and the prevalence was the same during the subsequent two years. Another pathologist working independently in Rabaul from 1964 onwards found a similar prevalence, (Kariks and McGovern, 1967) and since 1967 the prevalence of amyloidosis in the post mortems has remained at about 7%. (Wilkey, 1970). Champness (1962) performed approximately 100 post mortems in Rabaul during 1960-61. Histological sections from these were reviewed by the author and 6 cases of amyloidosis, probably all primary, were found.

The author found small deposits of amyloid in the kidneys of one of the 81 victims of accidental death, and Wilkey, too, encountered amyloid in one of approximately 100 similar forensic autopsies. This suggests that there is a significant amount of subclinical amyloidosis in the general population.

Any post mortem in which tuberculosis was found was excluded from the group of primary amyloidoses. In many of these cases however, the acute tuberculous infection may have been a terminal event rather than predisposing to the formation of amyloidosis. If this could be assumed, then the prevalence of primary amyloidosis in the autopsy series would be 4.4%.

Turnbull (1914), reporting a post mortem series from London before the advent of drug therapy for tuberculosis, recorded a prevalence of 0.66% of amyloidosis in 1,199 cases of tuberculous infections. He observed that amyloidosis was more liable to occur in patients with tuberculosis when there was chronic pulmonary cavitation, and involvement

of bones and joints. The prevalence of amyloidosis in his series of 129 cases of chronic pulmonary phthisis was 6.2% while the prevalence among 35 cases of bone and joint tuberculosis was 20%. Since neither of these two forms of tuberculosis was represented in the post mortem series from T.P.N.G., it seems reasonable to assume that most of the patients with tuberculosis and amyloidosis could still be regarded as being primary amyloidosis.

The prevalence of amyloidosis in patients dying from leprosy varies in different population groups, being 60% in the white patients in the U.S.A. (Shuttleworth and Ross, 1956); 50% in the Polynesians in Hawaii (Beddow and Tilden, 1960); while it is very rare in India (Cochrane and Davey, 1964). It certainly occurs in Australian aborigines (personal observation) but prevalence figures are not available. 60% of the leprosy patients included in the present post mortem series were shown to have amyloidosis.

2. Organ Distribution

In reviewing 53 cases of secondary and 20 cases of primary amyloidosis, Briggs (1961) concluded that there was no significant difference in the organ distribution between these two groups. In the present material no difference in organ distribution between the primary and the secondary cases of amyloidosis was apparent. There was however, a difference between the anatomical distribution in these cases and those of previously reported series of primary amyloidosis. In the series of non-familial primary amyloidosis reviewed by Symmers (1956); in Familial Mediterranean Fever (Sohar et al, 1967); and in the form of familial amyloidosis associated with urticaria and deafness

reported by Muckle and Wells (1962), heavy deposits of amyloid were present in the interstitial tissue of the kidneys, spleen and adrenals, while deposits in the liver were small and almost exclusively confined to the walls of small blood vessels.

In the T.P.N.G. cases the renal and hepatic involvement resembled this, but parenchymal involvement of spleen and adrenals was minimal. On the other hand, the presence of amyloid goitre was more common in this series than in those previously reported.

3. Clinical Syndromes in Primary Amyloidosis

Uraemia

Uraemia was the commonest mode of presentation. Almost all the patients were normotensive. As demonstrated in Chapter 3, a patient with chronic renal disease and normal blood pressure was very likely to be suffering from primary amyloidosis.

Amyloid Goitre

Amyloid goitre was the mode of presentation of two patients in this series. Amyloid goitre was present in a number of other patients with amyloidosis, and amyloid was present in all nine of the thyroids examined in post mortems of primary cases, and in four of the five thyroids examined in secondary cases.

Amyloidosis in Children

Amyloidosis occurring in children is very rare and the majority of cases reported since the advent of antibiotics have complicated Still's disease. (Strauss et al, 1969). In the present autopsy series there were five cases of secondary amyloidosis in

children, four associated with leprosy and one with tuberculosis. However, the association of chronic renal disease and an amyloid goitre appeared to constitute a definite clinical syndrome of primary amyloidosis which has not been recognised in other parts of the world.

Malabsorption and Cardiac Arrhythmia

Amyloidosis should be included in a differential diagnosis of malabsorption syndrome and of cardiac arrhythmia in patients in T.P.N.G.

4. Duration of the Illness

The average duration of the disease is recorded as being 8 weeks. Taken at face value this appears to be an extremely rapid progression of the disease. However, this cannot be regarded as being reliable because it was based on the clinical history, and people in T.P.N.G. had very little idea of time. There was positive proof that two patients survived for two years following the diagnosis of amyloidosis, while a third child is still alive four years after presenting with chronic renal disease and an amyloid goitre.

Pathogenesis

Cohen (1967) pointed out that three main mechanisms have been postulated for the pathogenesis of amyloidosis, namely an abnormality of plasma cell function, an immunological abnormality and genetic pre-disposition.

Only one patient in this series was suffering from multiple myeloma, and this was found to be a gamma D type (Hobbs et al, 1966).

Plasma cell abnormalities were specially looked for during 1966 and 1967 but none was identified.

Serum protein estimations have been made on a number of different population groups in T.P.N.G. (Brading, 1958; Curtain et al, 1965). These demonstrated a lower albumin level and a slightly higher gamma globulin level than occurs in normal Caucasians. The author arranged for the serum proteins to be measured in a number of different groups of patients including a group of normal indigenous residents of Port Moresby. The serum protein values of these normal indigenes did not differ significantly from the normal laboratory values for Caucasians. The patients with leprosy who had no evidence of amyloidosis had a raised gamma globulin, which appeared to be due to an increase in all three immunoglobulins. The patients with chronic renal disease not due to amyloidosis, and those with primary amyloidosis, had low serum albumin levels, presumably as a result of albuminuria. The patients with chronic renal disease not due to amyloidosis showed a moderate increase in IgM whereas those patients with primary amyloidosis showed a marked increase in IgM. Immunoglobulins have been estimated in two other groups of patients undergoing special investigation in T.P.N.G. Patients with Kuru showed no significant abnormality in immunoglobulins. (Chandor and Hornabrook, 1969). Patients with tropical splenomegaly showed elevation of their IgM levels and this was ascribed to the presence of antibodies developing as a result of infection with Plasmodium malariae. (Crane and Wells, 1967). The reason for the elevated IgM levels in the patients with primary amyloidosis has not been elucidated. However, this abnormality in immunoglobulins may indicate the presence of some abnormality in the immunological mechanism in these patients. Further study of the immunological responses of normal

inhabitants of T.P.N.G. and of patients with amyloidosis may demonstrate some abnormality which renders this population particularly liable to develop amyloidosis.

The finding of such a large number of cases of primary amyloidosis in young people in a population consisting of numerous closely knit clans, strongly suggested that a genetically determined abnormality similar to that found in Portugal (Andrade, 1952) and in Israel (Heller et al, 1958) would be found in this population also. So far there has been no evidence to support such an hypothesis. None of the cases in this study were blood relatives, although some came from neighbouring villages. Even up to the present time, in spite of continuing investigations, no two cases have been blood relatives (Anders and Wilkey, 1971).

In order to examine this possibility more closely, the author assisted in two surveys in which a medical team visited a number of villages near Port Moresby, from which patients with amyloidosis had been diagnosed. The urines of as many of the villagers as possible were examined for the presence of albuminuria, on the assumption that this would be the easiest method of detecting patients with sub-clinical amyloidosis. The intention was to admit to hospital for further investigation anyone with albuminuria. Two people who did exhibit albuminuria were admitted to hospital and rectal biopsies were performed. Both of these were negative. Although both of these preliminary surveys were disappointing, such surveys may be useful in identifying patients with sub-clinical amyloidosis.

Apropos of this, it was very interesting to note that Vines (1970) observed a relatively high prevalence of albuminuria in both males and females throughout the country. In the Mainland and Islands

regions, 5% of the 823 males and 4% of the 797 females tested, showed albuminuria greater than 100 mgms%. This was noted at all ages but was more prevalent in those over 15 years of age. The significance of this was not ascertained, but it is interesting to speculate that at least some of these people may be suffering from sub-clinical amyloidosis.

Because of the prevalence of parasitic and other infectious diseases, these were considered as possible causes of the amyloidosis. No evidence for this was found in the cases studied, and if they were to be important causes of amyloidosis, one would expect to find a similar prevalence in other tropical countries. This has not been the case.

Summary

Amyloidosis was found in 7.3% of 1,100 post mortems performed in T.P.N.G. between 1962 and 1967. At least half of these cases could be classified as primary amyloidosis. A prevalence such as this has not been reported from any other country.

This investigation has defined the problem of amyloidosis as it occurred in T.P.N.G. during the period studied. The clinico-pathological manifestations of the disease were identified and described. Nephropathy was the commonest presenting manifestation. This was frequently accompanied by an amyloid goitre. The combination of chronic renal disease and an amyloid goitre appeared to constitute a readily recognisable and unique, clinical syndrome in children.

The features of the amyloidosis occurring in T.P.N.G. were compared with those found in other countries. No specific aetiological

factor was identified, but a simple genetic cause can be virtually excluded. The patients tested showed elevated IgM levels, and further investigation of the immunological responses of the normal people, and of those suffering from amyloidosis, may reveal some abnormality which would explain the reason for this unique prevalence of amyloidosis, and possibly assist in the understanding of the pathogenesis of this condition.

CHAPTER 3

URINARY SYSTEM AND MALE GENITAL SYSTEM

Renal Disease

Each year from 1960 to 1964 renal disease was listed as the tenth most common cause of death in T.P.N.G., accounting for between 2 and 3.4% of the 2,500 deaths recorded annually. (Department of Public Health Hospital Disease Statistics, 1963 to 1964 (1967)). These figures were based on information derived from death certificates, some of which, particularly from small hospitals, were signed by medical orderlies. The figures are therefore of questionable significance because even under relatively sophisticated conditions of death certification, fewer than two thirds of cases are correctly diagnosed as renal disease. (Burry, 1966). No breakdown into the different types of renal disease was possible because very few of these cases were submitted to post mortem examination.

In an attempt to gain a clearer understanding of the prevalence of renal disease, its relative importance as a health problem, and in particular, the types of chronic renal disease most prevalent in the community, two studies were undertaken. Firstly, a review of the types of chronic renal disease admitted to the Port Moresby General Hospital, the largest in T.P.N.G., and secondly a review of the types of renal disease occurring in the post mortem material. (Cooke and Champness, 1968).

Material and Methods

Clinical Study

The Port Moresby General Hospital was the base hospital for the South Coast Region, and a wide range of patients was admitted. It was considered that the classification system of the medical records department was not sufficiently well organised for all cases of renal disease to be obtained by this means. Therefore, the records of all patients admitted with a blood urea greater than 60 mgms.% during the years 1962, 64, 65 and 66 were examined. These cases were selected by examining the daily work books of the biochemistry section of the Pathology Department. All the biochemical investigations performed in the hospital were recorded in these books, and this was thought to be the quickest and easiest way of finding the cases required for this investigation.

The case histories were examined by a physician (Dr. L. Champness) and by the author, in order to determine the clinical features of these cases, and to exclude cases in which the elevated blood urea levels were not due to renal disease. Dehydration due to dysentery was the commonest non-renal condition producing an elevated blood urea.

The diagnosis of the type of renal disease was considered positive when there was histological proof of this, or when, as in three cases, a clinical diagnosis could be confirmed by haematological or radiological examinations.

All the histological material was examined by the author. Chronic pyelonephritis was defined according to the criteria of Weiss

and Parker (1939). Cases were included under the heading chronic glomerulonephritis when virtually all glomeruli were abnormal, some being enlarged and hypercellular. In most of these cases epithelial crescents were also present. The diagnoses of amyloidosis, oxalosis, gout, polycystic disease and membranous glomerulonephritis were made when the well recognised features of these conditions were present in the histological sections. (No distinction was made between primary and secondary amyloidosis in either the clinical or the post mortem studies).

89 cases were finally selected. 16 of these came to post mortem examination and were therefore included in both the clinical and the post mortem studies.

Post Mortem Study

A survey of 880 post mortems performed throughout T.P.N.G. between 1962 and 1966 was made, and cases of renal disease of sufficient severity to be the main cause of death, were selected for study. Post mortems on neonates; non-indigenous residents; cases of sudden death due to accident, homicide and suicide were not included in this review. Disseminated tuberculosis and primary and secondary neoplasms were not included under the heading of renal disease. The histological sections of the kidneys were reviewed personally.

Results

Clinical Study

The 89 cases were divided into two groups, one hypertensive with blood pressures greater than 140/80 and the other normotensive

with blood pressures no greater than this. 45 cases were hypertensive and 41 were normotensive. Blood pressures were not recorded in three cases.

12 of the 89 cases exhibited features of the Nephrotic Syndrome.

Hypertensive Group

Positive diagnoses made on the hypertensive cases are shown in Table 6.

TABLE 6

Positive Diagnoses on 9 Hypertensive Chronic Renal Disease Cases

Histological examination of renal biopsies taken during life or at post mortem:

Chronic pyelonephritis	3
Amyloidosis	2
Chronic glomerulonephritis	1

Other examinations:

Disseminated Lupus Erythematosus (Clinical and haematological)	1
Polycystic kidneys (radiological I.V.P.)	1
Aortitis with coarctation-like constrictions and aortic incompetence (clinical and radiological)	1

Rectal biopsies were performed on a further 13 patients in this group, and congo red stained sections were examined under polarised

light. No amyloid was detected in any of these.

Normotensive Group

Positive diagnoses were made on 20 of the normotensive cases. The details of these are listed in Table 7.

TABLE 7

Positive Diagnoses on 20 Normotensive Chronic Renal Disease Cases

Post mortem examination of kidneys:	
Amyloidosis	11
Chronic pyelonephritis	1
Membranous glomerulonephritis	1
Biopsy examination:	
Rectal biopsy - Amyloid present	6
Renal and Thyroid biopsy - Amyloid present	1

One normotensive leprosy patient had no histological diagnosis, but would almost certainly have had amyloidosis.

Nephrotic Syndrome

Twelve of the 89 cases presented to the hospital with the features of the nephrotic syndrome. (Unfortunately the blood pressure recordings on these patients have been mislaid). In only four of these was a positive histological diagnosis made:

Amyloidosis	2
Membranous glomerulonephritis	1
Chronic pyelonephritis	1

Age and Sex Distribution

The age and sex distribution is shown in Fig.25(b). The male to female ratio was 2 : 1 and the majority of the cases were in the 11 to 30 years age range.

Prevalence of Chronic Renal Disease

The figures shown in Table 8 indicate that the prevalence of chronic renal disease among the hospital admissions varied very little during the 4 years studied. The average was 0.29% of the 30,460 admissions.

TABLE 8

Percentage of Chronic Renal Disease Among Hospital Admissions

	1962	1964	1965	1966	Totals
No. of Hospital Admissions	6,313	7,026	8,260	8,861	30,460
No. Chronic Renal Disease	17	20	27	25	89
% Admissions	0.27	0.28	0.33	0.28	

Post Moretm Study

103 cases of renal disease were found - 11.7% of the autopsies.

The diseases encountered are listed in Table 9.

TABLE 9

Renal Disease in 880 Autopsies

Amyloidosis	66
Chronic pyelonephritis	23
Chronic glomerulonephritis	4
Acute pyelonephritis	2
Oxalosis	2
Acute glomerulonephritis	1
Cytomegalo virus infection	1
Gout	1
Polycystic disease	1
Membranous glomerulonephritis	1
Acute bilateral renal vein thrombosis	1
	103

A detailed account of amyloidosis is given in Chapter 2. No difference was found in the regional distribution of amyloidosis. The regional distribution of the cases of renal disease other than amyloidosis is shown in Table 10. In these, too, there is no statistically significant difference between the prevalence in the various regions.

TABLE 10

Non-amyloid Renal Disease

	Total	South Coast	North Coast	Highlands	Islands
No. of Post Mortems	880	247	317	247	69
No. Cases	37	9	11	13	4
% of Post Mortems	4.2	3.6	3.5	4.8	5.9

Age and Sex Distribution

The age and sex distribution of non-amyloid renal disease is shown in Fig.25(a). The male to female ratio was 2.5 : 1, and the majority of cases occurred in the age range 11 to 30 years.

Discussion

Although only a relatively small number of patients admitted to hospital were suffering from renal disease, a significant number of deaths were due to this cause. The author's studies demonstrated that the commonest form of renal disease was amyloidosis. The commonest form of non-amyloid renal disease was chronic pyelonephritis. It can be inferred from the data presented, that the prevalence and the types of renal disease occurring, were similar in all parts of the country.

The clinical study demonstrated that patients suffering from chronic renal disease could be divided into two groups - one hypertensive and the other normotensive. Positive diagnoses were made on only 9 of the hypertensive cases. However, rectal biopsies performed on 13 further patients showed no evidence of amyloidosis. Rectal

biopsy has been shown to be a useful means of confirming a diagnosis of amyloidosis. Blum and Sohar (1962) obtained a positive result in 75% of 62 cases of proven amyloid disease. In the author's own series (Chapter 2), rectal biopsy was positive in 6 out of 8 patients with proven amyloidosis. It seems reasonable to assume, therefore, that amyloidosis was excluded in at least half of the patients with hypertensive chronic renal disease. On the other hand, half of those with normotensive chronic renal disease were shown to <u>have</u> amyloidosis.

Therefore, when a patient with chronic renal disease had a blood pressure less than 140/80, he was likely to be suffering from amyloidosis. This diagnosis would be further strengthened if the patient exhibited any of the other clinical manifestations noted in Chapter 2.

In previous studies of renal disease in T.P.N.G., amyloidosis was overlooked. Campbell and Arthur (1964) reported that 46 of 2000 admissions to the adult medical ward of the Port Moresby General Hospital between 1960 and 1962, were for renal disease. No mention of amyloidosis was made, although the importance of this condition was recognised during 1962. A later review of the hospital case records showed that some of the cases labelled as chronic pyelonephritis on clinical grounds, were shown to have amyloidosis at post mortem, but the post mortem report had not been inserted into the case notes by the Records Department. (personal observation).

Champness (1962) noted a high prevalence of renal disease in Rabaul during 1960-61. He performed approximately 100 autopsies during those 2 years, selecting in particular, patients who had died from renal disease. Reviewing the histology of these cases in 1963, the author

found that 6 had amyloidosis. Further analysis of the kidney sections of these autopsies was not possible because the histological slides were mislaid.

Kariks and McGovern (1967) described a form of progressive focal glomerulonephritis in 15 of 167 post mortems performed in Rabaul during 1965 and 1966. Amyloidosis was present in 4 of these cases.

Although these other studies of renal disease did not highlight the presence of amyloidosis, they support the contention that amyloidosis was indeed a common and important cause of renal disease.

Acute glomerulonephritis appeared to be relatively uncommon. Only 1 case was represented in the post mortem study. Campbell and Arthur reported only 1 case in their series, and paediatricians consulted about this, agreed that such cases were rare.

Acute tuberculous renal lesions consisting of varying numbers of small, miliary tubercles were commonly found at post mortem in patients dying of tuberculosis, but these lesions were not regarded as sufficiently severe to be a cause of death. No case of chronic tuberculous renal disease was encountered by the author, and the Director of Tuberculosis also commented on the rarity of this condition. (Wigley, 1967). Likewise, Campbell and Arthur did not observe any case of tuberculous renal disease.

Comparison with Other Countries

The features of renal disease found in this post mortem investigation were compared with those of a post mortem series in Australia (Burry, 1966) and in Uganda (Hutt and Sood, 1963). The

former was chosen as an example of an "industrialised" country, and the latter as an example of a country with similar environmental and social conditions to those in T.P.N.G. The main features of this comparison are illustrated in Table 11.

TABLE 11

Renal Disease in Post Mortems in Three Different Countries

	T.P.N.G.	Australia	Uganda
No. of post mortems	880	507	320
% of renal disease in the post mortems	11.7	8.3	17
Major type of disease encountered	Amyloidosis	Analgesic Nephropathy	Pyelonephritis

Detailed comparisons between post mortems performed in different countries are very difficult to make, owing to the differences in disease patterns, and the selection of patients for post mortem examination. (The Australian series quoted, for example, was from a hospital for adults, and so no children were included). Therefore, only general trends can be recognised.

Table 11 illustrates that renal disease formed a significant percentage of the autopsies performed in all three countries. Three different conditions were the commonest causes of death from renal disease in each country. Amyloidosis was the commonest renal disease in post mortems in T.P.N.G. No case of amyloidosis was encountered in the Australian series, and only two of the 55 cases from Uganda were due to amyloidosis. Analgesic nephropathy was the commonest disease

in the Australian series. No kidney with the features described in analgesic nephropathy was observed in the post mortem material from T.P.N.G. Analgesic abuse could be discounted as a contributing cause of chronic renal disease in T.P.N.G. because patent medicines were not freely available to the inhabitants during the period of this study.

Pyelonephritis, either acute or chronic, was the commonest cause of death from renal disease in Uganda, and approximately 2/3rds of these were due to urinary obstruction, particularly urethral stricture. Urinary obstruction was not found in any of the cases of chronic pyelonephritis included in the post mortem series from T.P.N.G. This may have been overlooked in a few cases because of the conditions under which many of these post mortems were performed. However, urinary obstruction due to calculus, neoplasm or stricture was seen only very rarely. (personal observation).

It is now recognised that the diagnosis of chronic pyelonephritis by the histological criteria used for this study is imprecise. (Heptinstall, 1966). No evidence of active infection was found in the cases labelled "chronic pyelonephritis", and therefore some doubt must be cast on this diagnosis. However, Vines (1970) found pyuria in between 3% and 7% of apparently healthy males from all parts of T.P.N.G. which must indicate that sub-clinical urinary tract infection was relatively common. Whatever the true aetiology of this group of cases, they accounted for a significant proportion of the renal disease. Further investigation may clarify this problem. Perhaps a form of nephropathy peculiar to T.P.N.G. may be identified.

Most of the cases from T.P.N.G., both in the clinical and in the post mortem study were under the age of 30. This only reflected

the age structure of the population at that time. The male to female ratio of cases resembled that seen in hospital admissions, and therefore did not indicate any difference in prevalence between the two sexes.

Nephrotic Syndrome

The cases of nephrotic syndrome included in the clinical study were not truly representative of nephrotic syndrome seen in the hospital, because all those selected had elevated blood ureas. A histological diagnosis was made on only four of the twelve cases included. Patients with nephrotic syndrome rarely came to autopsy because the course of this disease is relatively prolonged, and the practice was to discharge such patients so that they could die at home. Recently, a more extensive investigation of nephrotic syndrome was carried out in Lae on the North Coast (Powell and Meadows, 1970). 36 patients were investigated. Renal biopsy was performed on 29 of these. Three of the 29 had primary amyloidosis. The remainder showed a wide range of histological appearances including minimal change on light microscopy, focal proliferative glomerulonephritis, membranous glomerulonephritis and combinations of membranous and proliferative glomerulonephritis. Apart from the amyloidosis, the pattern did not show any striking differences from what has been reported from other countries (Kibukamusoke, 1968).

Although none of the 12 cases included in the present study were associated with infection with Plasmodium malariae, cases of nephrotic syndrome in whom this parasite was demonstrated in the peripheral blood were observed in the hospital during the period under study. (Maddocks and Booth, 1967). This association between nephrotic

syndrome and infection with Plasmodium malariae appeared to be similar to that noted in Africa. (Gilles and Hendrickse, 1960). Thus, apart from the facts that amyloidosis and P. malariae infections must be considered in the diagnosis of nephrotic syndrome in T.P.N.G., no significant difference between this condition as it occurs in T.P.N.G. and in other countries has yet been recognised.

Summary

Renal disease accounted for only a small number of admissions to hospitals throughout T.P.N.G., but it was more important as a cause of death. It was equally prevalent in all regions. Patients with renal disease who were normotensive were likely to be suffering from amyloidosis, and this was the commonest cause of renal disease.

A form of chronic pyelonephritis for which no satisfactory cause was found, was the second most commonly encountered type of renal disease. Chronic tuberculous renal disease was notably absent. Amyloidosis and Plasmodium malariae should be considered in the differential diagnosis of nephrotic syndrome in T.P.N.G.

Other Diseases of the Urinary Tract

Renal carcinomas - clear cell adenocarcinomas in adults, and Wilm's tumours in children occurred infrequently. Bladder carcinomas were also seldom seen. Biopsy specimens from 9 cases were submitted for histological examination in the two years 1966 and 1967. Tumours of kidney, bladder and other parts of the urinary tract were classified together in the tumour registry, and accounted for 1.4% of all cancers.

It was observed by many experienced clinicians that renal and vesical calculi, particularly the latter, were uncommon. One man who presented with renal colic in Port Moresby was shown to have cystinosis.

Male Genital System

Penis and Scrotum

The main infective lesions encountered were Donovanosis and Amoebiasis, and they are dealt with in Chapter 9. Scrotal elephantiasis is also mentioned in the same chapter.

Carcinoma of the penis accounted for 2.0% of all cancers in males. Circumcision was not widely practised, and perhaps more penile cancers than this might have been expected. (Fig. 26). These cancers were often far advanced when first diagnosed. (Fig. 27). They were squamous carcinomas.

Two squamous carcinomas of the scrotum were encountered. One of these was of the verrucous variety.

Testis

Epididymitis due to tuberculosis and to filariasis was seen from time to time in surgical specimens. (Fig. 28). Occasional sperm granulomata and epididymal cysts were also seen. One relatively common cause of testicular atrophy was Lepromatous Leprosy, in which accumulations of organism-filled histiocytes caused pressure atrophy of the seminiferous tubules.

Testicular tumours accounted for 0.7% of all cancers in males. Tumours of all varieties occurred: seminoma, teratoma, interstitial cell, and one case of an orchioblastoma with secondaries in the inguinal lymph nodes, and radiological evidence of a secondary in the right lung. (Fig. 29).

Prostate

Benign adenomyomatous hyperplasia of the prostate was seen, but was not common. Seventeen such surgical specimens were examined in the two years 1966 and 1967.

Prostatic carcinoma accounted for 0.8% of all cancers in males.

CHAPTER 4

ORAL CANCER

A wide range of pathological conditions affecting the oral cavity were encountered, but the most important of these was oral cancer. This form of cancer accounted for 15.8% of the malignant neoplasms reported to the tumour registry between 1958 and 1967. Skin cancer accounted for approximately the same percentage, and together they represented approximately one third of all malignant neoplasms.

Oral cancer was most prevalent among coastal dwellers. Only 5% of all the oral cancers reported came from the Highlands, although approximately half the total population lived there. This discrepancy appeared to be related to the habit of chewing betel (areca) nut. Approximately 90% of coastal dwellers, both male and female, chewed betel nut regularly, and from an early age. Until quite recently this practice was rare amongst Highlanders, probably because the betel nut did not grow there. (Atkinson et al, 1964).

The following is an account of the clinico-pathological features of oral cancer in T.P.N.G.

Material

Between 1958 and 1967 a total of 490 cases were reported to the tumour registry. The clinico-pathological features to be described, and the observations on verrucous carcinoma, were based on personal observations made on 315 of these cases which were examined in the Pathology Department, Port Moresby from 1962 to 1967.

Results

Clinical Features

The average age of the patients with oral cancer was 44 years, and the male to female ratio was 2.7 to 1. This did not constitute a significant difference in sex distribution because it was similar to the sex ratio of admissions to all the hospitals in T.P.N.G.

70% of the tumours occurred on the buccal mucosa, often with the floor of the mouth involved as well. 20% involved the tongue, and the remaining 10% occurred on the lip.

The tumours were commonly very advanced. In some, the whole surface of the buccal mucosa on one side was ulcerated when the patient first presented. (Fig. 30). Frequently a fistulous opening was already present. (Fig. 31). Figs. 32 and 33 show a very large fistula in which the anterior end of the opening consisted of a tenuous connection between the upper and lower lips which was broken during the operative resection.

The tumour illustrated in Fig. 34 had produced ulceration on the buccal mucosal surface, and penetrated deeply into the soft tissues of the cheek. Ulceration through the skin of the cheek was about to occur. (Fig. 35). Occasionally a relatively small area of ulceration was present on the buccal mucosa - perhaps 2-3cms in diameter - and this communicated with a large mass of tumour in the soft tissues of the cheek and floor of the mouth, in the region of the submandibular gland. This tumour mass may have measured 5-6cms or more in diameter.

Occasionally multiple sinuses, discharging caseous-looking material were present. (Fig. 36). This necrotic keratin could be

mistaken for pus from an Actinomycosis of the jaw, particularly if, as in the case illustrated, no ulceration could be seen on the buccal mucosa. In this case there was an area of grossly thickened buccal mucosal epithelium which, when the operative specimen was cut, could be seen to connect with a very large squamous carcinoma in the soft tissues of the cheek and floor of the mouth.

Pathology

In 66 cases of oral cancer treated by surgical excision in which the pathology was personally reported, the size of the tumour was measured and all lymph nodes submitted were examined histologically. The sizes of these tumours are shown in Table 12.

TABLE 12

Diameter of Mucosal Aspect of 66 Oral Cancers Treated Surgically

Site	No. Cases	Diameter (cms.)			
		< 2	2-5	5-8	> 8
Buccal mucosa*	43	2	31	9	1
Tongue	9	1	7	1	0
Lip	10	6	4	0	0

* No measurement was recorded in 4 cases.

These figures confirmed the large size, and presumably the fairly advanced stage of the neoplasms at the time of presentation for treatment. Those treated represented only a relatively small number

of all the cases of oral cancer. The rest were considered to be inoperable either because of their size, or because of poor respiratory function resulting from chronic chest infection.

The usual surgical treatment for carcinomas involving the buccal mucosa or the tongue, was local resection of the tumour, together with removal of the ipsilateral cervical lymph nodes. This was sometimes accompanied by removal of the contralateral supra hyoid lymph nodes at the same operation. Occasionally, bilateral block dissection of the cervical lymph nodes was performed. However, in 5 of the cases of buccal mucosa cancer, no lymph node resection was carried out. A meaningful assessment of the pattern of lymph node metastases was therefore impossible from the present material. Nevertheless, as shown in Table 13, some information could be obtained. In a significant number of cases no secondary tumour was found. The prevalence of secondary deposits decreased with the distance of the lymph node from the primary tumour, while an occasional metastasis was present in cervical nodes on the side opposite to the tumour.

TABLE 13

Pattern of Lymph Node Secondaries in 51 Oral Cancers Treated Surgically

Site of Primary Tumour	Buccal Mucosa	Tongue
No secondaries present	16	4
Combinations of secondaries present in cervical lymph node groups in individual cases:-		
Ipsilateral upper	11	2
Ipsilateral upper and ipsilateral submandibular gland	2	0
Ipsilateral upper and mid	8	0
Ipsilateral upper, mid and lower	1	0
Ipsilateral upper and contralateral upper	1	0
Contralateral upper	0	1
Bilateral, upper, mid and lower	0	1
Exact site could not be determined from the specimen	3	1
Total number cases	42	9

All 10 of the lip cancers (Fig. 37) were treated by local excision without node dissection, no enlarged nodes being felt at the time of operation. Only 9 tongue cancers were included in Table 13, because tongue cancers were usually far advanced, (Fig. 38) commonly with lymph node metastases which were often bilateral. In the majority of cases a biopsy only was taken to confirm the diagnosis, and to notify the tumour to the tumour registry.

Tumour invasion of the facial bones was not assessed histologically in all the surgical specimens, but Bassett (1967), who reviewed the x-rays of 140 cases of oral cancer presenting for surgery in Port Moresby, found x-ray evidence of such invasion in 77% of them.

This review included only 6 patients who came to autopsy. None of these had tumour extending below the clavicles, and only one case of extension beyond the head and neck was observed clinically by Mr. F. Smyth, the surgeon who performed most of the operations. In that instance pulmonary secondaries could be seen on radiological examination.

Histological grading of 73 tumours from which large blocks were available was attempted, and the results are shown in Table 14.

TABLE 14

Site of Primary Tumour		Histological Grade		
		1	2	3
Buccal mucosa:	No. cases (47)	22	20	5
	% cases	47	42	11
Tongue:	No. cases (16)	7	9	0
Lip	No. cases (10)	7	3	0

The grading system (1 to 3) well differentiated (1) to undifferentiated (3) as suggested by Wahi et al (1965) and adopted by the W.H.O. International Reference Centre for Oropharyngeal Tumours was used. The sections from 140 cases of squamous carcinoma of the

oral cavity from different parts of the world, which constitutes this reference material, were examined at the same time, so that the grading system would be in harmony with that used by the consultant pathologists on that panel. In Table 15, the histological grading of cancers of the buccal mucosa and lip from T.P.N.G. is compared with a series from India. (Wahi et al, 1965). In India, as in T.P.N.G., betel chewing is ubiquitous and buccal mucosal cancers are the commonest oral cancers encountered.

TABLE 15

Histological Grading of Oral Cancer in India and in T.P.N.G.

Grade	Buccal Mucosa				Lip			
	India		T.P.N.G.		India		T.P.N.G.	
	Cases	%	Cases	%	Cases	%	Cases	%
1	285	36.3	22	47	22	47.8	7	70
2	447	57.0	20	42	22	47.8	3	30
3	53	6.7	5	11	2	4.4	0	
Total	785		47		46		10	

The results for tongue cancers were not comparable because those in Wahi's series were divided into lesions arising from the anterior two thirds, and from the posterior one third. The data from T.P.N.G. did not allow of such a division, and the tumours were usually so large that such a division would not have been possible. None of the 16 cases was a grade 3 tumour, but many of Wahi's cases, particularly those involving the posterior third, were.

The histological appearances of these oral cancers varied quite markedly even within the same tumour. Often, the major part of the tumour was well differentiated, while in some areas the cells were relatively anaplastic. (Fig. 39(a) & (b)). Almost invariably there was a heavy cellular infiltrate in the lamina propria adjacent to the tumours. This consisted mostly of lymphocytes and plasma cells. An infiltration of eosinophils was also usual, and commonly this was very marked. (Eosinophil infiltration of the tissues removed surgically from Papuans and New Guineans was very common. The explanation for this was not clear. It did not necessarily correspond to an eosinophilia in the blood. (Personal observation). Frequently, foreign body giant cell reactions could be seen around areas of keratin in the lamina propria. Secondary deposits in the lymph nodes often resembled caseating tuberculous lymph nodes. (Fig. 40). This necrotic looking material was in fact necrotic keratin, and sometimes a node such as the one illustrated would have only a small rim of tumour cells at the edge of the necrotic keratin. As a response to the keratin, epithelioid cells and multinucleated foreign body giant cells were also commonly present. (Fig. 41).

Verrucous Carcinoma

This tumour was first characterised by Ackerman (1948). It consists of a warty-looking growth with an irregular, papillary surface. (Figs. 42; 46 - 51). It does not infiltrate the deep tissues in the same aggressive fashion as does the ordinary squamous carcinoma, and when the tumour is cut across, a distinct, wavy margin can be seen on its deep surface (Fig. 42). The histological appearance is equally striking and characteristic. There is gross epithelial hyperplasia with hyperkeratosis of the superficial layer. The rete ridges are bulbous with clearly defined inferior margins and minimal cellular atypia. (Figs. 43, 44 & 45). Metastatic spread to lymph nodes does not occur. This variety of oral cancer was recognised in T.P.N.G. (Cooke, 1969) and the illustrations are from personally studied cases.

Material and Results

29 cases of verrucous carcinoma were found among the 315 cases of oral cancer studied personally. 25 were males, and 4,females. The age distribution was similar to that for all forms of oral cancer except that the youngest patient in this group was 30. All the cases came from the Coastal areas.

Clinico-pathological Features

The clinical, macroscopic and histological appearances are illustrated in Figs. 42 - 51. The tumour on the buccal mucosal surface was almost always associated with the presence of leukoplakia on the adjacent buccal mucosa. The anatomical location of these 29 cases is shown in Table 16.

TABLE 16

Verrucous Carcinoma - Anatomical Location

Location	No. Cases
Labial commissure	12
Commissure plus buccal mucosa	6
Buccal mucosa	7
Lip	2
Tongue	2
	29

The tumours varied in size from 1cm to approximately 5cms in diameter. The largest tumour encountered by the author is illustrated in Figs. 50 and 51. The sizes of the tumours are shown in Table 17.

TABLE 17

Verrucous Carcinoma - Diameter of Lesions in cms.

Location	No. Recorded	Range	Mean
Labial commissure	8	1 - 3	2.0
Commissure plus buccal mucosa	5	2.5 - 5	3.7
Buccal mucosa	7	2 - 5	3.5
Lip	2		1.5
Tongue	2		2.0

Follow-up

9 of the twelve patients treated before 1965 were contacted. All were alive, two having survived 5 years, three for 4 years, and 2 each for three and two years respectively. (Table 18).

TABLE 18

Verrucous Carcinoma - Follow-up of Patients Treated Prior to 1965

	Years since Treatment					Lost to Follow-up	Total
	1	2	3	4	5		
No. cases alive with no recurrence		2	2	3	2	3	12

Discussion

Cases reported by other authors - Sorger and Myrden (1960); Duckworth (1961); Goethals et al (1963); Mittleman et al (1964); and Kraus and Perez-Mesa (1966) - resembled those reported by Ackerman. The cases from T.P.N.G. also exhibited similar pathological features. Although follow-up was incomplete, it would appear that the prognosis was also similar.

A number of striking differences however, were exhibited by the cases from T.P.N.G.

Firstly, this type of tumour accounted for 9% of all the cases of oral cancer seen in the pathology department from 1962 to 1967. This was a much greater prevalence than was found in any previous series - for example, the 4.5% of oral cancers seen at the Mayo Clinic (Goethals

et al, 1963) and the 1.7% of oral cancers at Hammersmith Hospital, London (Duckworth, 1961). It was especially surprising that no case of this form of oral cancer had been reported from India prior to 1969. (Recently however, the author examined a number of cases of verrucous carcinoma diagnosed in Indian patients being examined by Pindborg and his co-workers. (Pindborg, 1971).)

Secondly, the average age of the patients was 44 years and there was no statistically significant difference in sex incidence. Most of the previously reported cases were elderly males.

Thirdly, the commonest site for the tumour in other published series was the buccal mucosa and lower gingiva. In T.P.N.G. however, the majority of tumours involved either the labial commissure alone, or in association with the buccal mucosa. Many of the tumours in T.P.N.G. spread on to the skin of the face near the angle of the mouth, and there was marked leukoplakia of the buccal mucosa adjacent to the tumours.

Fourthly, many of the patients in previous reports were tobacco chewers or smokers, or were taking snuff by mouth, and the tobacco was thought to be carcinogenic. Tobacco was not added to the betel nut chewing mixture in T.P.N.G. (Atkinson et al, 1964). Slaked lime (made from coral or from shell) was the only additive used. It was carried in a gourd and added to the chewing mixture by means of a moistened stick, which was then wiped along the buccal mucosa and sucked clean as it was withdrawn through the lips. (Fig. 52). It is tempting to suggest that this method of chewing betel nut may in some way be the cause of verrucous carcinoma in T.P.N.G. It is different from the

manner in which betel nut is chewed elsewhere in the world. In other countries the betel nut is usually mixed with varying combinations of tobacco and other ingredients such as spices and chillis. (Pindborg, 1968).

The importance of this neoplasm in T.P.N.G. is two-fold. Firstly, it is a form of oral cancer which occurs with significant frequency, and it can be cured by local excision without the need for radical surgery.

Secondly, this group of patients could form the nucleus for observations on a naturally occurring experiment in chemical carcinogenesis, which could be transferred to the laboratory by the selection of an appropriate experimental model.

Biological Behaviour of Oral Cancer

It has been observed by radiotherapists and surgeons who visited T.P.N.G. during the years of the tumour registry survey, that the oral cancers there, appeared to behave in a more benign fashion than did oral cancer in Australia. As was shown from the tumour registry figures, oral cancer was more prevalent in T.P.N.G. than in Australia, and the anatomical sites of the cancers were different - involving particularly the buccal mucosa in the former, and the alveolus and floor of the mouth in the latter. In Table 19 a comparison has been made between three series of cases, from Australia (Fleming, 1968), India (Balasubrahmanyan et al, 1954) and T.P.N.G. (Cooke, 1969). In all three series, cancer of the lip was omitted because lip cancers tend to grow more slowly, and to metastasise less frequently than do

other oral cancers. Verrucous carcinomas were also excluded from the T.P.N.G. series because their prognosis was excellent and no cases were included in the other series.

TABLE 19

Features of Cases of Oral Cancer at Time of Treatment

	Australia	India	T.P.N.G.
No. cases	115	127	52
% with lesions 2cms diameter	77%	75%	94%
% with metastatic lymph node spread	51%	22%	57%

These series are not exactly comparable. Firstly, all the lesions in the Australian series were situated on the floor of the mouth and/or on the lower alveolus, while the majority in the other two series involved mainly the buccal mucosa. Secondly, the size of the lesion and the assessment of metastatic lymph node spread was made on a clinical examination in the Australian series, and on a pathological examination in the other two. The lower percentage of cases with metastatic lymph node spread in the Indian series may have been due to a more conservative approach to treatment by the Indian surgeons. This is supported by the relatively lower percentage of lesions less than 2 cms. in diameter at the time of treatment. The cases in the Australian series were on the average 20 years older than those in the other two series.

Taking the figures shown in Table 19 at their face value as representing the situation regarding the commonest form of oral cancer

seen in the three countries, there was a slightly greater percentage of cases with lesions greater than 2 cm. in diameter at the time of presentation for treatment in T.P.N.G. ($p = 0.03$). There was no difference between those from Australia and T.P.N.G. in the presence of lymph node metastases at that time.

Follow-up of patients in countries such as India and T.P.N.G. is not easy, and long term results of treatment are therefore difficult to assess. An attempt was made in T.P.N.G. to locate patients treated for oral cancer. At the end of 1967 the number of such cases followed was small, and no firm conclusions could be reached. The impression was that a very large percentage were already dead within five years of their operation. On the other hand, a few were found alive and well and free from tumour five years post-operatively. When sufficient numbers of cases are available it may be found that the five year survival rate will not be much different from the 22.5% found in Australia. (Fleming, 1968).

Thus, on the basis of this relatively crude comparison with oral cancer occurring in two other countries, there appeared to be only a marginal difference in the biological behaviour of oral cancer in T.P.N.G.

Discussion

Oral cancer was one of the commoner forms of malignancy in T.P.N.G. It resembled the oral cancer occurring in India in its prevalence and in its predilection for the buccal mucosa. This contrasted with what occurred in people of Western European extraction

among whom oral cancer was relatively uncommon, with tongue and floor of mouth being the commonest anatomical sites involved. (Atkinson et al, 1964). It has been assumed that these differences may be related to differences in smoking and chewing habits of different population groups. These habits are currently being investigated (Pindborg, 1968).

Betel nut is chewed because of its mildly euphoric effect. In India, and in other countries where it is commonly chewed, a wide variety of substances including tobacco, lime, chillis and spices are added to the chewing mixture. In T.P.N.G. on the other hand, lime is the only additive used.

Cohen and Smith (1967) reviewed the various attempts made to produce oral cancer experimentally in animals using varying combinations of substances found in chewing mixtures from different parts of the world. They reported their own observations on the application of Mainpuri tobacco (a substance chewed in the Uttar Pradesh region of India) to the buccal mucosa of the cheek pouches of monkeys. They were able to produce some epithelial atypia, but in common with all the previous investigators, they were unable to induce true oral cancer.

It has been observed that oral cancer is frequently associated with oral leukoplakia, i.e. a white patch on the oral mucosa which cannot be scraped off. Leukoplakia has consequently been regarded as being a pre-malignant condition. Surveys of the prevalence of oral leukoplakia in T.P.N.G. (Atkinson et al, 1964), (Pindborg et al, 1968) have shown a high prevalence among coastal dwellers and a low prevalence among highlanders, and this paralleled the prevalence of oral cancer. Pindborg and his co-workers are currently engaged in a long

term study of a number of large population groups in different parts of India to see whether leukoplakia is really a pre-malignant condition, and whether other conditions may also be pre-malignant.

When attempting to compare the features of oral cancer in different population groups, many difficulties arise.

Problems in Comparing the Features of Oral Cancer in Different Countries

1. Different anatomical sites are involved - floor of mouth and tongue in Europeans, buccal mucosa in betel nut chewing communities.

2. Varying terminology is used in defining the anatomical sites of the tumour.

3. Different combinations of anatomical sites are used by different authors.

4. The ages of cases differ - e.g. those in Australia are approximately 20 years older than those in T.P.N.G. This may affect fitness for treatment, particularly surgical treatment. The natural life expectancy of a forty year old Papuan or New Guinean may be different from that of a sixty year old Australian, and this may be important in assessing results of treatment.

5. The size of the tumour may be assessed clinically or measured on a surgical specimen. It is usually measured as the diameter of the ulcerated area on the oral mucosa. Apart from the technical difficulty of measuring a lesion in the mouth of a patient who may be suffering from trismus, this does not necessarily give an accurate indication of the actual size of the tumour. Perhaps the assessment

of size should include some indication of the mass of tumour present, and not just the diameter of the area of ulceration on the oral mucosa.

6. The assessment of lymph node metastases may be based on a clinical or on a pathological examination. This causes difficulties because some lymph nodes may be enlarged as a result of inflammatory reaction due to secondary infection of the ulcerated tumour, while small metastases may not have caused clinically detectable enlargement of the node. Also, the lymph nodes submitted to the pathologist depend on the type of operation favoured by the individual surgeon.

7. Histological grading of these tumours is fraught with many difficulties. Firstly, a number of different grading systems have been used. Broders (1927) introduced a 1 to 4 histological grading system, while the W.H.O. expert committee on oro-pharyngeal tumours (1965) adopted a 1 to 3 grading system.

Secondly, there is a difficulty in the grading of individual tumours. Poorly differentiated areas may be found in tumours which are otherwise producing large amounts of keratin, and could therefore be classified as being well differentiated.

Thirdly, to get a proper appreciation of the range of differentiation in any given tumour, large blocks are necessary. In countries such as Australia where the first line of treatment is radiotherapy, only small biopsy fragments are available for histological examination.

Fourthly, it is difficult to get a number of pathologists to give a consistent, unanimous grading to any individual tumour, either because the criteria for grading are not sufficiently well defined, or they are applied differently.

Until problems such as these are resolved, the maximum amount of information will not be obtained from comparing data collected in different parts of the world.

Summary

The clinico-pathological features of oral cancer in T.P.N.G. have been presented.

Within the limitations discussed, the features of oral cancer in T.P.N.G. were compared with those in other countries. The age incidence, the prevalence, the predilection for occurrence on the buccal mucosa, the pattern of lymph node spread and the histological grading, resembled that seen in oral cancer occurring in India where betel nut chewing was also extensively indulged in. In Australia, a country with people mainly of Western European extraction, oral cancer occurred in older people, and tongue and floor of the mouth were the commonest anatomical sites involved. Only a marginal difference was noted between the biological behaviour of oral cancer in T.P.N.G., India and Australia.

Verrucous carcinoma accounted for 9% of the oral cancers. This was a higher prevalence than in any other population group. The commonest site of its occurrence was on the labial commissures, on the buccal mucosa, or on both, in contrast to the ~~the~~ buccal mucosa and lower gingiva of previously reported cases. It was suggested that the practice of applying lime with a stick to the betel nut chewing mixture may have contributed to producing this particular anatomical localisation of the lesion. Since it was potentially curable by relatively

simple surgery, it was important for medical practitioners in T.P.N.G. to be able to diagnose it correctly.

CHAPTER 5

JAW TUMOURS & BURKITT'S LYMPHOMA

Jaw Tumours

Tumours involving the jaw bones appeared to be more prevalent in T.P.N.G. than in Australia. This impression, which was gained by surgeons and pathologists alike, was borne out by the fact that jaw tumours, excluding cases of Burkitt's Lymphoma, accounted for approximately 2% of the neoplasms notified to the tumour registry over the 10 year period 1958 - 1967.

Material and Results

Forty-one cases seen during these 10 years were reviewed by ten Seldam and Cooke (1968). The tumour types encountered are listed in Table 20.

TABLE 20

Jaw Tumours T.P.N.G. - 1958-1967

Ameloblastoma	30
Adeno-ameloblastoma	4
Osteogenic sarcoma	2
Fibrosarcoma	2
Calcifying Epithelial Odontogenic Tumour	1
Plasmacytoma	1
Giant cell granuloma	1
	41

Ameloblastomas

The age and sex distribution of the 30 Ameloblastomas is shown in Table 21, while their anatomical sites are indicated in Table 22.

TABLE 21

Age & Sex Distribution
30 Cases of Ameloblastoma

	Age Groups (years)				
	15-20	21-30	31-40	41-50	51+
Males (14)	1	7	4	0	2
Females (16)	3	3	7	2	1

TABLE 22

Anatomical Sites
30 Cases of Ameloblastoma

Mandible	19
Maxilla	9
Unspecified	2

They presented clinically as large tumours of the jaw. (Fig. 53). They were usually multicystic and an "egg shell like" crackling could be felt over the various loculi. X-ray revealed a multicystic tumour. (Fig. 54). When cut across, the loculi were displayed. These contained fluid which was usually gelatinous and either clear or blood-stained. (Figs. 55,56 & 57). The range of histological appearances was similar to that

demonstrated in standard text books.

Adeno-ameloblastomas

All 4 Adeno-ameloblastomas were in the maxilla. Two patients were males and two were females. One was 3 years, two were 10 years and one was 25 years of age. They presented as uniloculated cystic swellings of the maxilla, sometimes associated with an unerupted tooth. (Figs. 58 & 59(a)). Histologically they showed odontogenic epithelium forming acini, and small amounts of amorphous, eosinophilic dentine both lining the acini, and dispersed through the clumps of odontogenic epithelial cells. (Fig. 59(b)).

Other Tumours

The calcifying epithelial odontogenic tumour, one of the rarest varieties of jaw tumours, was first described by Pindborg (1958). The case in this series presented as a unilocular cyst of the mandible in a 13 year old girl. (Fig. 60). It showed the characteristic histological appearance of clusters of small, rather cuboidal cells, with rounded masses of amyloid, and small, calcified bodies in the stroma of the tumour. (Fig. 61(b)). (Cooke and Toohey, 1969).

During the years 1968 to 1970 a number of other jaw tumours were referred to the author. Most of these were tumours other than ameloblastomas. They included Fibromas of various types, Myxoma, a further Osteogenic Sarcoma and a Rhabdomyosarcoma.

Discussion

This brief description demonstrates the prevalence and variety

of jaw tumours occurring in T.P.N.G. A relatively high prevalence of jaw tumours has also been reported from other tropical countries (Davies, 1959), but no satisfactory explanation for this has as yet been put forward. Apart from the difference in the prevalence, and in the size attained before treatment is sought, there appears to be little difference between jaw tumours occurring in tropical and in non-tropical countries. (Lucas, 1964).

Burkitt's Lymphoma

This tumour syndrome which particularly affects young children, was first described in Central Africa (Burkitt, 1958). 55% of 557 cases presented with a tumour involving one or more quadrants of the jaw. 25% presented with an abdominal tumour either alone or associated with a jaw tumour. The histological appearance of these tumours was remarkably constant and they appeared to be a form of malignant lymphoma. They differed from malignant lymphomas in other parts of the world in that they rarely involved the lymph nodes or the spleen. Although 80% of cases presented with either jaw or abdominal tumours,

6.8% presented with paraplegia from involvement of the spinal cord;

4.3% with thyroid tumours; and

3% with salivary gland tumours.

38% of the females presented with bilateral ovarian tumours and

3.8% of the males with testicular tumours.

This tumour syndrome has now been accepted as a specific form of malignant lymphoma characterised by its anatomical distribution and its histological appearance (Burkitt and Wright, 1970).

Burkitt Lymphomas have been identified in almost every country, but T.P.N.G. is the only place where anything approaching the prevalence seen in Africa is encountered (Burkitt and Wright, 1970). The first report of cases from T.P.N.G. was published in 1966.(ten Seldam et al, 1966). The author was a member of the team investigating this condition and the following is a review of the studies made on Burkitt's Lymphoma in T.P.N.G.

Material and Results

The age and sex distribution of 37 personally studied cases is shown in the histogram (Fig. 62). The majority occurred in children, and the peak age incidence was five years. All except three came from lowland coastal areas. (Fig. 63). A little over one-third of them presented as jaw tumours, (Figs. 64 & 65), and a further one-third as an abdominal mass, either retroperitoneal or involving the bowel. The remainder presented with tumours at other sites, for example the orbit (Fig. 66), both ovaries (Fig. 67) and in the spinal canal producing paraplegia. Only a small number of autopsies were performed. In one autopsy performed personally, tumour was found in the kidneys (Fig. 68), stomach (Fig. 69), thyroid, pancreas and testes, with sparing of the organs of the reticulo-endothelial system.

Histologically (Figs. 70 & 71), the tumours were fairly uniform in appearance, being composed of rather regular lymphoblast type cells. In the majority of the tumours, large, pale, histiocytes were scattered among the tumour cells. This feature gave rise to a "starry sky" appearance when histological sections were examined under low power. Imprint preparations made from some of these tumours

showed the characteristic cytological appearances of Burkitt's Lymphoma (Wright, 1967).

Radiological examination (Fig. 72) revealed bony destruction with a rather "moth eaten" appearance together with the soft tissue swelling adjacent to the bone.

Tissue Culture and Serology

Cells from two tumours were established in tissue culture. These were morphologically identical with cells cultured from African cases. Electron microscopic examination revealed Herpes virus-like particles which were also similar to those seen in African cases. (Fig. 73), (Epstein et al, 1967). These viruses were shown to be E.B. viruses of the type associated with Infectious Mononucleosis. Using these cells as antigen, human sera collected from various parts of T.P.N.G. were tested for complement fixing antibody to E.B. virus. The sera were all tested at a dilution of 1/8. (Pope, 1970). The results are shown in Table 23.

TABLE 23

E.B. Virus Antibodies in Normal People from T.P.N.G.

Age (years)	No. Tested	No. Positive
0-1	11	6
1-2	11	11
1-5	32	32
6-10	4	4
11-15	-	-
16-20	7	7
20+	18	17

Treatment

No figures are yet available concerning the response to treatment of patients in T.P.N.G. The author was not personally involved in the treatment of any patients, but was able to observe the response to treatment in approximately 12 cases. Figs. 74 and 75 illustrate the response shown by one patient, one week after an intravenous dose of Endoxan. A number of other patients likewise had a good immediate response to cytotoxic drugs. Some patients had a partial response, but the tumour was beginning to re-grow at the time of discharge two or three months after the first treatment. Some patients were moribund on admission to the hospital, and they died shortly afterwards. A few patients were referred to the Queensland Radium Institute for treatment by radiotherapy. This produced an excellent immediate remission, but the long term results were not seen, as the patients were repatriated at the end of their course of therapy.

Discussion

The tumour syndrome occurring in children in T.P.N.G. resembled in all respects the features of Burkitt's Lymphoma. As was found in the African cases, almost all those from T.P.N.G. came from areas below 4,000 feet altitude, and this supported Burkitt's hypothesis that an infective agent, possibly transmitted by an arthropod vector may be involved in the causation of the tumour. (Booth et al, 1967).

Almost all the people tested, including those with Burkitt's Lymphoma had antibodies to E.B. virus. In these preliminary screening tests there were insufficient sera to determine whether there was any

difference in prevalence of the antibody in highland or lowland populations. The significance of these results is very difficult to assess. They could mean that the whole population has been exposed to infection with this virus, and that a few susceptible children developed a malignant lymphoma as a result. However, while the virus particles have been demonstrated in tissue cultures, they have not shown any biological activity, and they may be passenger viruses rather than causative agents.

Burkitt and Wright (1970) were able to review the survival of 60 African patients treated with cytotoxic drugs. 26% of these survived longer than 2 years. It would seem likely that follow-up of New Guinea patients will reveal a similar survival rate.

Many questions about Burkitt's Lymphoma remain unanswered - one of the more interesting of these is why it is comparatively common in only two countries in the world which are so widely separated geographically.

Summary

In this chapter the features of jaw tumours occurring in T.P.N.G. have been described. Special attention was focused on Burkitt's Lymphoma because T.P.N.G. is the only country in which it occurs with anything like the frequency encountered in Africa.

CHAPTER 6

ALIMENTARY SYSTEM

Salivary Glands

Tumours and mucocoeles were the only two conditions seen frequently by the pathologist. The "mixed" type of salivary gland tumour (pleomorphic adenoma) was the one most commonly encountered (Fig. 76), but a great variety of histological types were represented. Tumours of the minor salivary glands and the lacrymal gland were seen from time to time.

Mucocoele

Mucocoeles were sometimes excised because a clinical diagnosis of neoplasm had been made. They consisted of a unilocular cyst, filled with semi-solid, mucoid material. Histologically they were not encapsulated, and the cyst lining consisted of granulation tissue through which were scattered numerous foamy histiocytes (Fig. 77). It seems probably that the mucocoeles resulted from obstruction to ducts as a result of trauma. Exact numbers are not available, but they were relatively common in the surgical pathological material from T.P.N.G., as compared with similar material from Brisbane, Australia. The difference in prevalence may be related to the trauma inflicted on the facial region from sleeping on hard ground, fighting etc. One member of the author's staff developed a mucocoele in a parotid gland about three weeks after he had fallen down an embankment on his way home from a pay-day "spree". He appeared quite normal prior to his fall, but when

he came to work a few days later, his face was swollen and showed signs of abrasions. About a month after this he attended Outpatients, where he was seen by a surgeon recently arrived from Australia. In due course his parotid gland came to the laboratory, having been excised because of an erroneous diagnosis of salivary gland tumour.

Oesophagus

Oesophageal pathology was rarely encountered. A few malignant neoplasms, and one giant leiomyoma were submitted for histological examination.

Stomach

Tumours

Malignant neoplasms of oesophagus and stomach accounted for 4.5% of the tumours registered from 1958-1967. They did not exhibit any features specifically relating to their occurrence in T.P.N.G.

Peptic Ulcer

There were 23 gastrectomy specimens in a series of 5,500 routine surgical specimens examined during 1966 and 1967. All of these operations were performed for complications of chronic peptic ulcers - haematemesis, pyloric obstruction, severe pain or perforation. The analysis of these cases according to age and sex is shown in Table 24.

TABLE 24

Gastrectomies for Complications of Peptic Ulcer

	Age Groups (years)			
	25-30	31-40	41-50	51+
Males (19)	4	6	7	2
Females (4)	0	2	1	1

The pathological features of these peptic ulcers were no different from those encountered in other countries.

These cases almost certainly represented only a small percentage of the total number of patients suffering from peptic ulceration. It would be impossible to ascertain the exact prevalence of the disease, because Papuans and New Guineans had a high threshold for endurance of pain; there were often language difficulties in history taking; and facilities for performing barium meal examinations were available in only one or two centres. It is interesting to note, however, during 1968 at the Royal Brisbane Hospital, 39 gastrectomy specimens for chronic peptic ulcer were received in the Pathology Department among a total of 10,000 routine surgical specimens. Thus, peptic ulceration may be no less prevalent among Papuans and New Guineans than among Australians.

Small Intestine

Enteritis Necroticans

Enteritis necroticans (necrotising enteritis) or, as it is

called locally, "Pig-Bel", is a condition which has provoked widespread interest. It was first reported from the Highlands by Murrell and Roth (1963). It usually occurred in children and young adults. The patients presented with symptoms and signs of acute intestinal obstruction. Loops of thickened, tender bowel could often be palpated through the abdominal wall. During the years 1962-1963, and 1966-1967, the author examined 38 cases of "Pig-Bel".

Pathology

The lesion consisted in a segmental enteritis which involved one or multiple segments of the small intestine, with the jejunum being most severely affected . (Fig. 78). The bowel was usually dilated, with thickening of its wall, and mucosal ulceration. (Fig. 79). There was usually haemorrhage into the bowel wall, and this resulted in the bowel looking a black colour. Frequently there were frankly gangrenous areas in the bowel wall, and perforation, often at multiple points, was a common complication.

The whole thickness of the bowel wall was involved by an acute inflammatory process (Fig. 82(a) & (b)). The mucosa was ulcerated, and gram positive bacilli were often present in the purulent exudate lining the mucosal surface. Thrombosis of the small submucosal vessels was frequently seen.

Age and Sex Distribution

TABLE 25

Age and Sex Distribution of 38 Cases of Enteritis Necroticans

	Age Groups (years)						
	0-5	6-10	11-15	16-20	21-30	31-40	41+
Males (30)	10	10	1	0	4	3	2
Females (7)	1	2	0	2	0	2	0

No age or sex was recorded in 1 case

Geographical Distribution

Cases were encountered from all parts of T.P.N.G. and the geographical distribution of the author's cases is shown in Table 26.

TABLE 26

Geographical Distribution of 38 Cases of Enteritis Necroticans

Highlands	23
Wewak area on the North Coast	7
Other centres on the North Coast	2
Islands Region	3
British Solomon Islands	2
Daru on the South Coast	1
	38

Necrotising Colitis

Five cases were encountered in which an identical pathological appearance to that described above was found in a segment of colon. All of these were males between 30 and 40 years of age, and all presented as acute abdominal emergencies. The diagnosis of necrotising colitis was made at laparotomy, and the diseased segment of colon was excised. Three of these cases came from the Highlands, and two from the Wewak area on the north coast.

Pathogenesis

Murrell (1967) investigated cases of "Pig-Bel" occurring in the Highlands. He postulated that the condition was caused by the ingestion of contaminated pork eaten during ritual pig feasts. These feasts were arranged at irregular intervals throughout the Highlands to celebrate important occasions in the lives of the various tribes. At such times large numbers of pigs were killed, and after being partially cooked, they were eaten at some time during the subsequent few days.

A Clostridium welchii, type C, was isolated from the bowel contents of a number of cases of "Pig-Bel". This organism was not a normal bowel inhabitant, and it was postulated that it may have been the cause of the disease. However, this organism could not be isolated from pigs, or from samples of pork.

The author's experience demonstrated that "Pig-Bel" was not confined to the Highlands, but occurred in many other parts of T.P.N.G.

Many of these patients denied having eaten pork prior to the onset of symptoms, even on specific questioning about this.

It seems, therefore, that other factors apart from the ingestion of contaminated pork may be involved in the aetiology of "Pig-Bel". The cases of necrotising colitis appear to fall into the same spectrum of disease, but their cause also is not known.

Phlegmonous Enteritis

During 1969, Doctor I. Wilkey and the author encountered three adult males aged 20, 35 and 40 years respectively, who presented as acute abdominal emergencies with symptoms and signs of small intestinal obstruction. Laparotomy on all three patients revealed similar pathology. Each had a segment of the mid or lower ileum which was thickened and dilated. The abnormal segments, which were usually one or two feet in length, were resected, and all the patients recovered satisfactorily following the operation.

The segments of bowel were dilated, with grossly thickened walls (Figs. 80 & 81). The thickening was mostly submucosal with some hypertrophy of the muscle layers. Histological examination revealed an intact mucosal epithelium with gross distension of the submucosa by oedema, by polymorphs or by a mixture of the two. (Fig. 83 (a) & (b)).

The cause of this condition was not ascertained. The patients all came from different parts of the country, one from the Highlands, and one each from the north and south coasts. There was no obvious common factor in the clinical history. The pathological features were different from those seen in "Pig-Bel", and they appeared to constitute

a separate entity which has been tentatively labelled "phlegmonous enteritis".

Tuberculosis

This condition is dealt with in Chapter 9.

Other Infections

Typhoid fever was seen fairly commonly, and the diagnosis was confirmed by culture of the organism from one or all of faeces, blood and urine. Only a few cases were seen among the autopsies.

Nematode infestations, particularly Hookworm and Ascaris were extremely common. Occasional cases of acute intestinal obstruction, particularly in children, were due to a matted mass of Ascaris worms. This complication was encountered especially after treatment of a very heavy infestation with anti-helminthic drugs.

Tumours

The commonest tumour encountered in the small intestine was Malignant Lymphoma. These presented either as an abdominal mass, or because of intestinal obstruction caused by intussusception of a polypoid mass of tumour. In a few cases there was more than one discrete area of tumour. (Fig. 84).

Appendix

Acute appendicitis was certainly seen in 1962 and before this, but only a few specimens were submitted for histological

examination in 1962-63. Many more were being submitted, particularly from Port Moresby, in 1967. Whether this indicated a rise in prevalence, or whether it simply meant that surgeons had decided not to discard appendicetomy specimens is a little difficult to determine.

One case of acute amoebic appendicitis was encountered. As so often happens in these rare cases, the patient died of the ensuing peritonitis because the diagnosis was not suspected prior to histological examination of the appendix.

Large Intestine

The commonest colonic disorder encountered was dysentery. The organism most commonly isolated, both in Port Moresby and in Wewak was Shigella flexneri (Curtis, 1964; Morahan, 1968). Other shigellas and various salmonellas were also isolated. Cases of amoebic dysentery and amoebomas of the rectum, and less commonly of the caecum, were also encountered. The diagnosis in these cases was made by finding the Entamoebae either in faeces or in rectal biopsy specimens. Less frequently the organisms were found on histological examination of bowel removed because of a mistaken diagnosis of carcinoma. No case of ulcerative colitis or Crohn's disease was diagnosed during the period under study.

Volvulus of the recto-sigmoid appeared to be extraordinarily rare in view of the frequent post mortem observation of a relatively long mesocolon with bowel distended by bulky faeces resulting from the vegetarian diet.

Carcinoma of caecum, colon, rectum and anus occurred with

reasonable frequency but they did not present any features peculiar to their occurrence in T.P.N.G. Two conditions occurring in T.P.N.G. which can be wrongly treated as carcinomas are amoeboma and tuberculoma. Examples of both conditions treated by partial colectomy were submitted for histological examination.

Pancreas

A few cases of acute pancreatitis were seen during life and at post mortem. A few cases of carcinoma were also seen.

A survey conducted by Price and Tulloch (1966) revealed an incidence of diabetes of 0.1% in 3 village groups around Port Moresby. An incidence of 1.4% was found in a fourth group which had had contact with Europeans since 1874. Even this figure was low when compared with the incidence in many other countries. No case of diabetes appeared in the author's autopsy series.

No case of fibrocystic disease of the pancreas was diagnosed during the period under study.

Gall Bladder

Gall stones were rarely encountered. Occasionally small pigment calculi were found at post mortem, and on one occasion an incidental finding was the presence of numerous "mixed" calculi in intra-hepatic bile ducts. Likewise, only a few cases of chronic cholecystitis such as the one in Fig. 85 were seen in the surgical pathological material.

One case of acute gangrenous cholecystitis was seen in a male aged approximately 25 years who was dead on arrival at the hospital in Port Moresby. Pseudomonas aeruginosa was isolated in pure culture from the bile and from an associated pneumonia. There were no calculi; and no special cause for the unusual gram negative septicaemia was found.

Summary

The following were the most important observations: Salivary gland tumours of all types were frequently encountered. Mucocoeles of the major salivary glands appeared to be relatively common.

Twenty three gastrectomies for complications of chronic peptic ulceration were performed. There appeared to be little difference in the prevalence of this condition in T.P.N.G. as compared with Australia.

A series of cases of enteritis necroticans was reviewed. This condition was originally reported from the Highlands where it usually followed the ingestion of partially cooked pork. In this present series, however, cases came from all parts of the country, and in some there was no history of recent ingestion of pork. Five cases of segmental colitis were encountered in which the clinico-pathological features resembled those seen in enteritis necroticans. The aetiology of these cases was not ascertained.

Attention was drawn to the occurrence of another condition affecting the small intestine which caused acute intestinal obstruction. This has been tentatively labelled "phlegmonous enteritis".

Dysentery, caused by a variety of infectious agents, was the commonest colonic lesion.

Pancreatic and biliary tract pathology were rarely encountered.

CHAPTER 7

LIVER DISEASE

Cirrhosis and Hepatoma

One of the most striking pathological conditions encountered by the first European trained pathologists to work in tropical countries was the prevalence of cirrhosis and hepatoma. Experience of these two conditions in tropical Africa, India and South East Asia was published by Berman (1951). Attention was drawn to the occurrence of these two conditions in T.P.N.G. by Backhouse (1955). He reported finding 6 cases of hepatoma (all in cirrhotic livers), and 6 cases of cirrhosis without hepatoma in a series of 1050 autopsies performed in Rabaul between 1923 and 1940.

In the earliest reports from Africa, the prevalence of cirrhosis was somewhat exaggerated, because cases showing periportal fibrosis accompanied by varying degrees of mononuclear inflammatory cell infiltration were also included under the heading of cirrhosis. This finding is very common in the livers of the indigenous inhabitants of many tropical countries (Higginson, 1957). It is very commonly found in T.P.N.G. also, both in biopsy and post mortem material (personal observation). McGovern and Kariks (1966) reviewing 117 post mortems in Rabaul, found such changes in 93 of the 117 livers, and concluded that this process was an early stage of cirrhosis. A longitudinal study such as that being undertaken by Blackburn (1968) may throw more light on this condition. In this study, apparently healthy volunteers are being followed over a period of years. Patients are being examined

clinically, and liver function tests and liver biopsies are being performed. Preliminary results, however, have not yielded any definitive conclusion as to the relationship, if any, between the periportal fibrosis and cirrhosis. The practical importance of this histological appearance of the liver is that unwary pathologists, confronted with liver biopsies from tropical countries, could regard these changes as being abnormal. As far as can be ascertained, however, they are not necessarily associated with demonstrable abnormality of liver function.

What follows is a review of the author's experience of cirrhosis and hepatoma in T.P.N.G.

Material

Sections of livers from 880 post mortems received in the Pathology Department, Port Moresby between 1962 and 1966 were reviewed. Post mortems on neonates, expatriates and unnatural causes of death were excluded. There were 58 cases of cirrhosis and 36 cases of hepatoma.

250 liver biopsies obtained by percutaneous needle aspiration were received in the department during the same period. These sections were also reviewed. There were 27 cases of cirrhosis without hepatoma, and 48 cases of hepatoma.

Results

Among the post mortem sections there were 31 cases in which cirrhosis was present alone without any associated hepatoma. These cases were combined with those needle biopsies which showed cirrhosis

only. The age and sex distribution of 54 of these cases is shown in Fig. 90 (a). (No age or sex was known for 4 cases).

The age and sex distribution of 78 of the 84 cases of hepatoma from the combined post mortem and biopsy series is shown in Fig. 90 (b). The age and sex of the other 6 cases was not known.

Both conditions showed a similar age and sex distribution. Both cirrhosis and hepatoma occurred in young children, but most cases occurred during adult life.

The prevalence of cirrhosis and hepatoma in post mortems performed in the four geographical regions of T.P.N.G. are shown in Table 27.

TABLE 27

Regional Prevalence of Cirrhosis & Hepatoma in T.P.N.G.

	South Coast	Highlands	North Coast	Islands
No. post mortems (880)	247	247	317	69
No. cases cirrhosis (58)	13	21	18	6
% of post mortems	5.3	8.9	5.7	8.7
No. cases hepatoma (36)	8	12	13	3
% of post mortems	3.2	4.8	4.1	4.3

There appeared to be no statistical difference between the prevalence of these two conditions in different parts of the country.

Pathology

In only a relatively small number of cases was the whole organ examined in Port Moresby. When not complicated by hepatoma, the livers were a little smaller than normal, with a coarsely nodular capsular surface. On the cut surface the nodules were characteristically a yellow colour, and varied in size from a few millimetres to 1 cm. in diameter. (Figs. 86 & 87). The nodules were separated by bands of fibrous tissue which were sometimes quite wide.

The livers containing hepatomas were usually enlarged, often grossly. The commonest macroscopic appearance was that of multiple rounded foci of tumour occurring throughout the liver (Fig.88). Massive tumours replacing either the right or the left lobes were also seen. Tumour thrombi completely obstructing the portal vein and the terminal portion of the inferior vena cava were noted in some cases (Fig. 89).

Because most of the autopsies were performed by doctors unskilled in this procedure and working under very difficult conditions, the pattern of metastatic spread of the hepatomas could not be determined. However, microscopic invasion of hepatic veins was seen in many cases, as were also pulmonary secondaries.

The hepatomas were classified histologically as hepatocellular, bile duct type, and mixed if they showed both patterns. The results of this histological classification are illustrated in Table 28.

TABLE 28

Histological Types of 84 Hepatomas in T.P.N.G.

Hepatocellular	(a)	32
	(b)	42
Mixed	(a)	4
	(b)	6
Bile duct type		0

(a) Post mortem series (b) Biopsy series

Prevalence of Hepatoma as Compared with Other Tumours

Hepatomas accounted for 31% of 125 post mortems on patients dying of malignant disease. This was a highly selected group of malignant neoplasms. A more realistic figure was the 6% of 3,085 malignant neoplasms notified to the tumour registry from 1958 to 1967.

Comparison with Other Countries

A comparison between the prevalence of cirrhosis and hepatoma in a number of different countries is shown in Table 29.

TABLE 29

Cirrhosis and Hepatoma in Different Countries

	United Kingdom[1]	U.S.A.[2]	India[3]	South African Bantu[4]	T.P.N.G.
No. post mortems	7,217		5,803	876	880
% Cirrhosis	1.5	1.6	3.5	5.0	6.6
% Hepatoma	0.3	0.35	0.46	3.0	4.1
% Cirrhosis complicated by Hepatoma	16.5	4.8	13	44	46

1. Dible (1957); 2. Steiner (1957); 3. Wahi (1957); 4. Higginson (1957).

The prevalence of cirrhosis and hepatoma in T.P.N.G. resembled that seen in the South African Bantu. The results from India occupied an intermediate position between the United Kingdom and the U.S.A. on the one hand, and Africa and T.P.N.G. on the other.

The sex incidence of cirrhosis and hepatoma in three countries is shown in Table 30.

TABLE 30

Sex Incidence of Cirrhosis and Hepatoma

	United Kingdom		South African Bantu		T.P.N.G.	
	M	F	M	F	M	F
Cirrhosis	1.7	: 1	4.3	: 1	3.4	: 1
Hepatoma	4.5	: 1	8.8	: 1	3.4	: 1

There was no significant sex difference in the prevalence of

these two conditions in T.P.N.G., but hepatoma showed a slight male preponderance in the United Kingdom, and a very marked male preponderance in Africa.

80% of the hepatomas from T.P.N.G. were of the hepatocellular type. This compared with 90% in the South African Bantu, and 54% of those from the United Kingdom.

Discussion

Prior to 1964, the medical staff thought that liver disease, in particular cirrhosis and hepatoma, was more prevalent in the Highlands than elsewhere. The present investigation showed no difference in prevalence in different parts of the country.

The macroscopic appearance of the cirrhotic livers indicated that they were almost exclusively of the macronodular type of cirrhosis, which was different from the predominantly micronodular cirrhotic livers seen in Australia (personal observation). The macroscopic appearance of the hepatomas did not differ from the macroscopic appearances in other countries.

The prevalence and the pathological features of cirrhosis and hepatomas in T.P.N.G. resembled those seen in Africa, but were somewhat different from those seen in non-tropical "Western" countries.

Berman (1951) found that 81% of 826 malignant neoplasms diagnosed among South African Bantus between 1925 and 1944 were primary liver cancers. He quotes Snijders and Straub (1923) and other authors, as finding a prevalence of hepatoma of 33% and 41.6% of all malignant neoplasms among Chinese and Indonesians respectively. These early

reports of the prevalence of malignant neoplasms among the people of Africa and South-east Asia were based on post mortem material. As was the case in the material from T.P.N.G., this gave a falsely high prevalence of hepatoma. Tumour registries which have been set up in recent years give a more realistic assessment, for example, 6% of 1,573 malignant neoplasms in Uganda, in Africa. (Davies, 1959).

The aetiology of cirrhosis is still not known. The two most popular hypotheses are post-infective and nutritional (with or without the addition of alcohol). (Sherlock, 1968). In T.P.N.G., Acute Hepatitis was seen fairly commonly by clinicians, and occasional cases of acute or subacute necrosis were found at post mortem. Reliable figures relating to the prevalence of hepatitis in T.P.N.G. were not available. Dietary deficiencies were also widespread (Bailey, 1963; Hipsley and Kirk, 1965). Alcohol did not appear to be a complicating factor in T.P.N.G. at the time of this investigation, because alcoholic beverages only became freely available after 1966, and it was not customary for the people to make home-made alcoholic drinks. Thus, either hepatitis or malnutrition or both are probably the important aetiological factors in T.P.N.G.

The first reports of the greater prevalence of hepatoma among the inhabitants of tropical countries, (Berman, 1951) pointed to a possible environmental carcinogen. Aflatoxin can produce hepatomas in experimental animals, (Sherlock, 1968) but no naturally occurring carcinogen has yet been identified in man.

Summary

The pathological features of cirrhosis and hepatoma in

T.P.N.G. have been defined. These two conditions occurred commonly, and without any apparent difference in prevalence in different regions. Their prevalence and pathological features were similar to those seen in tropical Africa, and their prevalence was greater than in non-tropical countries whose inhabitants are of European descent. Alcohol did not appear to be an important factor in producing cirrhosis.

Miscellaneous Conditions

Kwashiorkor

Kwashiorkor occurred in young children in most parts of T.P.N.G., but the impression of clinicians was that it was more prevalent in the Highlands than elsewhere. The irritable child, with a flaky skin, ascites, oedema and sparse, fine hair (Fig. 91) was a fairly characteristic and pitiable sight. Such children showed gross fatty infiltration of their livers accompanied by a variable degree of periportal fibrosis.

Congenital Hyperbilirubinaemia

Nine patients with congenital hyperbilirubinaemia were reported by Vaughan et al (1970). Seven of these had the features of Dubin-Johnson (Sprinz-Nelson) Syndrome and two of the Rotor Syndrome. Six of the Dubin-Johnson cases were diagnosed in the Madang area during the year 1967, and only two of these were blood relatives. The seventh case was from Samarai on the south coast, and the diagnosis was made in 1966. A further case was diagnosed in Lae in 1968 (Powell et al, 1970).

Presenting Clinical Features

Case 1: Male 30 years. Eyes noted to be yellow by employer.

Case 2: Male 35 years. Admitted for treatment of a squamous carcinoma of lower leg and incidentally noted to be jaundiced.

Case 3: Female 22 years. Noted to be jaundiced during an antenatal examination.

Case 4: Female 15 years. Noted to be jaundiced while visiting a sister in hospital. The latter was not jaundiced.

Case 5: Female 28 years. Noted to be jaundiced during pregnancy. Had had two previous admissions to the hospital because of abdominal pain, the cause of which was undiagnosed. She was a sister of Case 4.

Case 6: Female 14 years. Noted to be jaundiced during treatment of an intercurrent infection.

Case 7: Female 17 years. Noted to be jaundiced at a routine medical examination upon admission to a convent to begin training as a religious sister.

Case 8: Male 40 years. Admitted for investigation of right sided upper abdominal pain, jaundice and pyrexia. At laparotomy for probable obstructive jaundice, the common bile duct was normal and the gall bladder showed chronic cholecystitis and contained two large pigment calculi.

The two patients with the Rotor Syndrome were both aged

17 years. One was a male and the other was a female. They were both referred for medical examination because they were noted to be jaundiced. Liver biopsies were normal and contained no excess of pigment.

Family Histories

Apart from the two sisters (Cases 4 & 5) there was no definite information on familial incidence. One other patient reported that his dead mother had been jaundiced, but histories were so unreliable as a result of language difficulties, that actual physical examination would have been necessary in order to get reliable genetic data.

Biochemical Investigations

All 8 patients with Dubin-Johnson Syndrome had elevated serum bilirubins ranging from 3.3 to 6.4 mg.%, with one reported as 13.3 mg.%. Almost all of the bilirubin was direct reacting (i.e. conjugated). Serum alkaline phosphatase and serum glutamic pyruvic transaminase levels were normal in all cases. In only one (Case 9) was an adequate bromsulphthalein excretion test performed. This showed 13% retention at 45 minutes and 26% retention at 210 minutes. When repeated a few days later, the figures were 7% and 25% respectively.

Liver Biopsy

This investigation was performed on all 8 cases, and the biopsies were examined by the author. The findings were similar in all of them. The liver appeared black in comparison with normal liver (Fig. 92). The liver architecture was normal. There were large amounts

of brown pigment in hepatocytes throughout all parts of the hepatic lobules, and in some cases there was pigment in Kupffer cells, and to a lesser extent in the portal tracts as well. (Fig. 93). Special stains to elucidate the nature of the pigment gave the following results:- prussian blue, negative; ammoniacal silver, strongly positive; sudan black B, negative. The pigment was rapidly removed in the presence of the oxidising agent potassium permanganate. These staining results were compared with those of two Australian cases from the files of the Royal Brisbane Hospital. The pigment in the latter cases did not stain with ammoniacal silver, and it was bleached much more slowly by potassium permanganate. These latter staining reactions are those usually found in previously described cases of Dubin-Johnson Syndrome (Dubin, 1958; Sherlock, 1968). The staining reactions in the cases from T.P.N.G. suggested that this pigment may have been melanin.

Summary

These cases resembled previously reported cases of Dubin-Johnson Syndrome, except for the variation in the staining properties of the hepatic pigment. The finding of 6 cases in one relatively small area in a single year, suggested that the condition was unusually prevalent in that area. Search for further cases, and detailed family studies on such cases would be likely to yield very interesting results.

Lobar Pneumonia

Jaundice was a common complication of lobar pneumonia both among Africans (Gelfand and Lewis, 1942) and among Papuans and New Guineans (Campbell and Arthur, 1964). The clinico-pathological features

of this association in T.P.N.G, were studied by Radford et al (1967). The changes they reported in liver biopsies included "cloudy swelling, individual and focal liver cell death, with and without an inflammatory cell response, focal reticulin collapse, evidence of liver cell regeneration, mononuclear cell infiltration in portal tracts, and appearances consistent with infectious hepatitis". They concluded that these changes could be described by the term "non-specific reactive hepatitis". They did not think that the prevalence of jaundice in cases of lobar pneumonia was specifically a reaction peculiar to the livers of Africans and New Guineans, but that it simply reflected a greater severity of respiratory infection, and would occur in any people with similar environmental conditions and standards of living.

In post mortems on patients dying of lobar pneumonia, the liver often showed congestion with some collapse of the reticulin framework around central hepatic veins, but the author was unable to detect any specific abnormality.

Tropical Splenomegaly

This consists in gross splenomegaly of uncertain cause (Fig. 94) associated with increased red cell destruction and red cell pooling in the spleen, together with an increased output of red cells from the marrow. This condition was present in many areas of T.P.N.G. (Pitney et al, 1968). Liver biopsies performed on African patients with a similar condition revealed varying degrees of infiltration of sinusoids and portal tracts by lymphocytes, together with hyperplasia of Kupffer cells. (Marsden et al, 1965). A similar phenomenon was described in T.P.N.G. (Marsden et al, 1967) and (Pitney et al, 1968). A histological

section from one of the author's cases is illustrated in Fig. 95.

Infections

Hepatic tuberculosis was sometimes a diagnostic problem. Campbell (1966) reported two cases of tuberculoma of the liver which mimicked hepatomas. The liver was occasionally involved as part of a miliary tuberculosis. In two patients encountered by the author miliary tubercles were found on liver biopsy when there was no evidence of pulmonary tuberculosis. Both presented severely ill with fever and enlarged, tender livers. The only abnormal liver function test was an elevated alkaline phosphatase. Liver biopsy revealed the presence of multiple tubercles. Both patients recovered with anti-tuberculosis therapy.

Amoebic abscesses of the liver were fairly common in most parts of T.P.N.G. The pathologist was often asked to try to find E. histolytica trophozoites in aspirated pus, or in biopsy material taken from the edge of an abscess during aspiration. Trophozoites could not always be found, particularly if the patient had received antiamoebic therapy for a few days prior to aspiration. When examined at post mortem, these abscesses were either uniloculated or multiloculated (Fig. 96), and this was also the experience of clinicians who treated the abscesses by aspiration. The abscess contained pus, but there was usually no fibrous tissue capsule. The pus merged into necrotic tissue, granulation tissue, and then healthy liver cells surrounding the abscess. Trophozoites were found most easily in the transition zone at the edges of the abscess. (Fig. 97).

Veno-occlusive Disease

No case of this disease which was first reported from the West Indies (Stuart and Bras, 1957) was recognised in T.P.N.G.

CHAPTER 8

SKIN TUMOURS

Malignant neoplasms of the skin accounted for 18% of the tumours notified to the tumour registry. They equalled tumours of the oral cavity as the commonest tumours notified. The tumour types in order of frequency were: squamous cell carcinoma, malignant melanoma, basal cell carcinoma and Kaposi's sarcoma.

Material

The following account was based on a review of the skin tumours in T.P.N.G. from 1958-1966. This was originally prepared and presented by the author to a regional meeting of the International Union Against Cancer. (Cooke et al, 1967). The melanomas encountered during 1967 were included in the review of melanoma presented here.

Squamous Cell Carcinoma

The anatomical sites of 401 squamous cell carcinomas of the skin are shown in Table 31.

TABLE 31

Anatomical Sites of 401 Squamous Cell Carcinomas of Skin

Lower leg	256	Hand	6
Foot	68	Neck	6
Scalp	11	Abdomen	6
Arm	9	Miscellaneous other sites	39

Total: 401

43% of the tumours occurred in the 31-40 years age range, and the male to female ratio of cases was 2 : 1.

The geographical distribution of those occurring on the lower leg and foot is shown in Table 32.

TABLE 32

Geographical Distribution Squamous Cell Carcinomas Lower Leg and Foot

	South Coast	Highlands	North Coast	Islands
Lower leg (256)	44	18	83	111
Foot (68)	9	9	24	26

On first looking at these figures it appears as though the squamous cell carcinomas were more common in the Islands region than elsewhere. This difference may be more apparent than real, however, because during this period there was a much higher reporting rate per head of population for all tumours from this region than from any other region.

Pathology

The majority of these tumours were very large before the patients presented for treatment. (Figs. 98, 99 & 100). Usually they were straight-forward squamous cell carcinomas histologically, but in some cases a large hyperkeratotic lesion of the lower leg, would show only pseudo-epitheliomatous hyperplasia on a biopsy taken from its edge. This was a confusing, but well recognised phenomenon. (Atkinson

et al, 1962). Sometimes many blocks had to be taken, particularly from the central portion of the tumour, before the characteristic pattern of squamous cell carcinoma could be found. Even when this was done, there still remained a group of lesions in which radiological examination revealed marked bony erosion of the shaft of the tibia. Histological examination of such tumours showed only marked epithelial proliferation with hyperkeratosis and bulbous rete ridges, and none of the usual features of an infiltrating squamous cell carcinoma. (Fig. 101). In the author's opinion, such lesions must be regarded as being examples of the verrucous type of squamous carcinoma similar to that seen in the oral cavity. (Chapter 4).

Pathogenesis

The fact that 64% of the squamous cell carcinomas occurred on the lower leg, and 17% on the feet, suggested that trauma was important in their aetiology. Tropical ulcer affecting the lower leg was commonly encountered, and prolonged trauma to these ulcers may have induced malignant change. In Africa, too, squamous cell carcinoma of the lower leg was one of the more common tumours, and trauma was thought to be an important cause. In support of this proposition, it has been noted that squamous cell carcinoma of the lower leg is uncommon among American negroes. (Davies, 1959).

Squamous cell carcinomas were seen in burn scars, (Fig. 102) and prolonged trauma may be important in these, too.

Albinism was relatively common. It is well known that Albinos are especially prone to develop squamous cell carcinomas, and this

complication was occasionally seen in T.P.N.G. (Fig. 103).

One child with Xeroderma pigmentosa, a well known premalignant condition of the skin, developed squamous cell carcinomas on the skin and also on the lips and on the cornea of the right eye. (Fig. 104).

Treatment

Even though the lesions on the legs were so large, surgeons found by experience that whenever possible, local excision with skin grafting was a more satisfactory form of treatment than amputation. Amputation of a lower limb was a very serious matter for people whose legs were their only means of "transport". Moreover, clinical observations, supported by inguinal lymph node biopsy at the time of surgical treatment of the leg tumour, showed that a significant number of such patients did not have secondary tumour metastases at the time of treatment. (personal observation).

Basal Cell Carcinoma

During the five years, 1962-1966, 18 cases were diagnosed by histological examination. (Fig. 105). The male to female ratio was 1 : 1, and the average age was 36 years (range 24-60 years). As can be seen from the reports of other tumours, this one was by comparison quite rare. 9 of the 18 cases came from the Highlands region where the level of ultra-violet radiation was fairly constant throughout the year, being slightly above the intensity recorded during summer in Western Queensland. (Robertson, 1967).

The comparative rarity of basal cell carcinomas in T.P.N.G.

could perhaps be explained by the fact that the pigmentation of the skin afforded some protection against the carcinogenic effects of ultra-violet irradiation. However, because the ultraviolet irradiation was greater in the Highlands than in the coastal areas, a noticeable difference between the prevalence of basal cell carcinomas in the two areas might have been expected.

This low prevalence of basal cell carcinoma of the skin was also noted among negroid people in Africa (Davies, 1959). Basal cell carcinoma of the skin is a very common affliction of white people living in tropical and subtropical areas such as Queensland, and in T.P.N.G. itself. (personal observation). The conclusion that skin pigmentation provides protection against ultra-violet irradiation, and therefore against the development of basal cell carcinomas, appears to be inescapable.

Malignant Melanoma

This tumour accounted for 2.4% of the malignant neoplasms reported to the tumour registry. The anatomical sites in which the melanomas occurred are listed in Table 33.

TABLE 33

Anatomical Sites of 75 Melanomas 1958-67

FOOT:	Sole of foot	16
	Foot - exact site not specified	14
	Heel	14
	Big toe	5
	Second toe	1
	Fifth toe	1

TABLE 33 (continued)

Anatomical Sites of 75 Melanomas 1958-67

LOWER LEG	3
INDEX FINGER	1
MIDDLE FINGER	1
HEAD: Eyelid	1
Scalp	1
Parotid gland area	1
Skin of cheek	1
Oral mucosa over hard palate	2
Tongue	1
BREAST	1
ANUS	1
ANUS AND VAGINA	1
SECONDARIES - NO PRIMARY FOUND:	
Inguinal lymph nodes	4
Cervical lymph nodes	2
Axillary lymph nodes	2
Site of biopsy not specified	1
	75

Examples of melanomas occurring in the different sites are shown in Figs. 106-111.

Of these 75 cases, 40 were males and 35 were females. The average age was 42 years, the youngest being 19 and the oldest 62.

The geographical distribution of the cases is shown in Table 34.

TABLE 34

Geographical Distribution 75 Melanomas 1958-67

South Coast	Highlands	North Coast	Islands
8	37	13	17

Conclusions

Three striking features emerged from this analysis. Firstly, half the melanomas were reported from the Highlands region which had the lowest overall reporting rate for all tumours. Further, 29 of these 37 melanomas were reported from the western and southern Highlands districts, where the medical services were the least developed in the whole of T.P.N.G. during the period of this survey. No particular difference in anatomical site or sex prevalence was noted in the melanomas from the Highlands, as compared with those from other parts of the country.

Secondly, 68% of the melanomas occurred on the feet, the majority being on the plantar aspect.

Thirdly, 9 cases (12%) presented with primary tumours involving a digit such as the big toe (Figs. 108 & 109) or a finger (Fig. 110). Nearly all of these were submitted for histological examination with a clinical diagnosis of "gangrenous digit".

Discussion

Melanomas were relatively common among Africans, and the commonest site for these was the soles of the feet. Primary involvement of a digit was not so prominent a feature as in T.P.N.G. It was also noted that melanomas occurred less frequently among American negroes than among indigenous Africans, and that the foot was not a particularly common site for melanoma in the former group. This led to the suggestion that trauma played an important role in both the prevalence, and the special site predilection of melanomas among indigenous Africans. (Davies, 1959).

Recently, a survey was made of the pigmentation of the feet of members of the different tribes in Uganda. (Lewis, 1968). A high incidence of discrete areas of pigmentation of the soles of the feet was found. Histologically these were junctional naevi or lentigos. The incidence of these areas of pigmentation closely followed the different tribal incidence of melanoma of the foot.

In T.P.N.G. trauma could be invoked as an aetiological agent because the people wore no protective footwear, and the country is rugged and the terrain rough. This would not however, explain what appeared to be an especially high prevalence in the western and southern Highlands.

The whole tumour was seldom submitted for histological examination. Flat, pigmented areas separate from the main tumour were present in two of those that were submitted. (Fig. 111). Histologically these areas were either junctional naevi or lentigos. (Fig. 113). The prevalence of pigmented areas on the soles of the feet of normal people

in T.P.N.G. is not yet known.

A survey of melanomas among the people of Queensland, Australia (Davis et al, 1966) can be quoted for comparison. The people of Queensland are mostly of European descent, with social customs and living standards vastly different from those obtaining in T.P.N.G. In the series from Queensland, 34% of the tumours occurred on the trunk, and 33% on the legs. Only 3 of the 400 tumours occurred on the sole of the foot, and there were only 2 subungual melanomas, one on the hand and one on the foot. The back was the commonest site for the primary lesion in males, while the legs were the commonest site in females. No such difference in the site of the primary tumour was seen in the two sexes in T.P.N.G.

The biological behaviour of melanoma in T.P.N.G. is not known. Information about this would necessitate careful history-taking and follow-up of patients, and this was virtually impossible under existing conditions. As with other lesions, the melanomas were quite large when the patient first presented for diagnosis and treatment, as can be seen from the tumours illustrated. This, too, contrasts with the Australian cases where over 80% of them were 2 cms. or less in diameter when the patient first presented for diagnosis.

Summary

The features of 75 cases of melanoma in T.P.N.G. are presented. 68% of these occurred on the feet. 12% involved primarily a digit. There appeared to be a particularly high prevalence in the western and southern Highlands. The features of the tumours in T.P.N.G. resembled

those occurring in Africa, but were quite different from those occurring in Queensland, Australia.

Kaposi's Sarcoma

Only 4 cases of Kaposi's sarcoma were recognised up to 1967. The first of these, a male aged 25 years, had multiple lesions on the toes and dorsum of the right foot (Fig. 114). There were also isolated lesions on both thighs and on the back. (Biggs et al, 1963). The second, a male aged 37 years, from the same locality, had multiple lesions on both hands and on his left foot. (Fig. 115). The other two, both males aged 25 years, had single lesions, one on the upper arm and the other on a finger. Each of these cases came from different localities.

The histological appearances of the tumours showed no features different from those of previously recorded series.

This tumour occurred less frequently than might have been expected from the prevalence reported among Uganda Africans. (Hutt and Wright, 1968).

Benign Tumours and Other Skin Lesions

Many skin adnexal tumours were examined, but no special records of them were kept.

Benign naevi were very infrequently seen in the surgical pathological material, probably because the people did not request their excision. The author observed them on the skin of many individuals,

but no special survey was carried out.

Albinos were comparatively common in this population. (Fig. 116). Walsh (1967) recognised two types - the pure albino, and albinos with small, pigmented patches on various parts of the body surface. He called the latter "spotted" albinos. A further abnormality of skin pigmentation noted was the "red-skin". Both forms of albino were prone to develop skin cancers, but the "red-skins" had no particular sensitivity to light.

Occasional cases of many other skin conditions were noted, for example the young girl with disseminated lupus erythematosus. (Fig. 117). No special record of these were kept.

Infective lesions were frequently encountered, and these are dealt with in Chapter 9.

Summary

An account is given of the skin tumours encountered in T.P.N.G. They equalled oral cancer as the commonest malignant neoplasm notified to the tumour registry.

Squamous cell carcinomas were the commonest type. They occurred most frequently on the lower leg and foot. A group of cases was identified as the so-called "verrucous type" of squamous carcinoma.

Basal cell carcinomas were rare, and no increased prevalence was noted in the Highlands, as might have been expected on account of the high intensity of ultra-violet irradiation there.

Melanomas occurred particularly on the feet. 12% of those

reported involved primarily a digit, and there appeared to be a comparatively high prevalence in the western and southern Highlands.

Kaposi's sarcoma was encountered, but it was much less prevalent than it is in Africa.

CHAPTER 9

DISEASES DUE TO PATHOGENIC ORGANISMS

Infective diseases were very important in T.P.N.G. From 1963-1966 they accounted for 50% of hospital admissions, and for 56% of hospital deaths throughout the country. (Vines, 1970). Leprosy and malaria were commonly encountered but no specific pathological features related to their occurrence in T.P.N.G. were noted. In this chapter special emphasis is placed on diseases whose clinico-pathological features are less well known, or in which the author contributed to the elucidation of the clinico-pathological features of the disease as it occurred in T.P.N.G.

Amoebiasis

The prevalence of clinically recognisable disease due to infection with the parasite Entamoeba histolytica was difficult to assess from statistics based on hospital reports, because the parasite was not positively identified in all cases recorded as Amoebiasis. In the author's experience, this parasite was the cause of a small number of cases of acute dysentery, a considerable number of hepatic abscesses, a few amoebomas of rectum and caecum, an occasional case of acute appendicitis, and an occasional case of acute intestinal obstruction due to an inflammatory mass in the ileo-caecal region. All of these conditions exhibited clinico-pathological features which have been well documented in the medical literature.

Cutaneous Amoebiasis

In T.P.N.G. cutaneous manifestations of Amoebiasis were seen very frequently. Although exact prevalence figures were impossible to obtain, it was certainly the commonest manifestation of amoebiasis seen in the laboratory. From informal discussions with pathologists and clinicians from other countries in which amoebiasis is prevalent, the author formed the impression that cutaneous amoebiasis was more prevalent in T.P.N.G. than elsewhere. For this reason, a knowledge of the clinico-pathological features of this manifestation of the disease is mandatory for any medical practitioner in T.P.N.G.

Material

The following account is based on cases personally diagnosed on histological examination of biopsy material. Unfortunately the exact number of cases was not recorded, but examples of the various manifestations of this condition are illustrated.

Results

This form of amoebiasis occurred in all parts of T.P.N.G. Both sexes were affected. Most of the cases were young adults. The youngest patient encountered was a paraplegic girl aged about 10 years, who had a lesion involving the labium major and the groin.

The ano-genital region was the commonest site in both sexes.

Anal Amoebiasis

In the anal region it produced a heaped up, hard mass with

raised edges which completely encircled the anus. (Figs. 118 & 119). The condition was painful for sitting and walking. Spread to adjacent skin was occasionally seen. (Fig. 120). In one patient a recto-vaginal fistula had developed.

Genital Amoebiasis

Male

Amoebic balanitis occupied third position after gonorrhoea and donovanosis as a cause of venereal disease. The organism lodged beneath the prepuce. The resulting oedema and accumulation of pus caused dysuria, and sometimes acute retention of urine. This was relieved when erosion through the prepuce occurred. (Fig. 121). Left untreated, further erosion of the shaft of the penis occurred, (Fig. 122) and then the suprapubic area became involved. (Fig. 123). There was usually a copious amount of pus.

Female

Lesions occurred in the groins, (Figs. 124 & 125) on the clitoris (Fig. 126), on the vulva, and also producing a vaginitis and cervicitis (Fig. 127). The vulval lesions were sometimes associated with amoebic vaginitis and cervicitis as they were in the case illustrated in Fig. 124.

Diagnosis

Until the clinical features of this condition became known to practitioners in T.P.N.G. following the investigations of Cooke and

Rodrigue (1964), an erroneous diagnosis of squamous carcinoma was almost invariably made. The lesion was either biopsied or, as shown in (Fig. 119), a complete excision was performed.

The histological appearances were as confusing to the pathologists as were the clinical appearances to the clinicians. There was usually a very marked pseudoepitheliomatous hyperplasia, often so marked as to resemble closely the appearance of a squamous carcinoma; and many experienced pathologists made this mistake when shown sections of these lesions. (Figs. 128 & 129). The trophozoites of E. histolytica were usually present in large numbers in the pus on the surface of these lesions. The parasites could be found relatively easily if one searched with a scanning lens for a crack in the epidermis. (Figs. 130 & 131). At these sites pus with large numbers of parasites was usually encountered.

When this condition was suspected clinically, the diagnosis could be easily confirmed by examining a wet preparation of the pus smeared from the surface. Actively motile trophozoites of E. histolytica were readily found by this means. Alternatively a biopsy was quite satisfactory for confirming the diagnosis.

Treatment

These lesions all responded quickly to anti-amoebic therapy. Emetine was the main drug used until quite recently when Flagyl came into use. Within two days of beginning treatment improvement was clearly obvious, and the lesions were usually cured within two to three weeks of treatment being started.

A number of cases of amoebic balanitis were treated by

circumcision. This cured the condition, and follow-up of a small number of such patients a few months post-operatively showed that no recurrence had occurred.

Pathogenesis

When sexual partners had amoebic vaginitis and amoebic balanitis, infection appeared to be by sexual contact. Such was the case in the couple reported by Mylius and ten Seldam (1962). Presumably the amoebae spread from the anus of the female to the vagina, and the male was infected from the amoebic vaginitis.

In none of the cases reported by Cooke and Rodrigue (1964) was vaginitis found in the sexual partners of males with amoebic balanitis. Infection in these cases could have occurred from coitus per rectum. When infection involved the groins, the mode of infection may have been from faecal contamination of this area. However, it was noted repeatedly that patients with cutaneous amoebiasis were not suffering from amoebic dysentery, nor could active trophozoites of the parasite be found in stool examinations, although E. histolytica cysts were occasionally found.

The exact mode of infection thus remained unexplained. Also unexplained was the reason why the skin became liable to infection in the first place, and why this form of amoebiasis appeared to be uniquely prevlaent among the people of T.P.N.G.

Summary

All forms of amoebiasis occurred in T.P.N.G. but cutaneous

lesions involving the ano-genital region appeared to be particularly prevalent. The reason for this was not determined.

Filariasis

Wuchereria bancrofti was the species of filarial worm found throughout the coastal areas of T.P.N.G. Microfilariae were commonly seen in blood films of patients who had no clinical evidence of filariasis. Pathological changes associated with the lodgement of adult worms in large lymphatic channels resulted in lymphadenopathy and elephantiasis. These manifestations occurred in only a small proportion of the population exposed to infection.

The commonest sites of filarial elephantiasis were: scrotum (Fig. 132), vulva (Fig. 133), breast (Fig. 134), legs (Fig. 135), and arms. Lymphadenopathy, of the inguinal (Fig. 136) and less commonly of the supratrochlear nodes was encountered. These nodes felt rubbery, and when cut across, nodules of lymphoid tissue separated by bands of fibrous tissue were seen. (Fig. 137). Dilated lymphatic vessels were also present. (Fig. 138). Adult worms were found coiled up in some of the dilated lymphatics. (Figs. 139 & 142). Eosinophils were often present in large numbers, sometimes forming eosinophil "abscesses". The worms ultimately died and became calcified. A feature not stressed in accounts of the histological appearances of filarial lymphadenopathy was the occasional presence of "tubercles" resembling those in tuberculous lymphadenopathy. (Figs. 140 & 141). No acid fast bacilli were found in these areas, but adult filarial worms were demonstrated elsewhere in the node. The adult filarial worms were not always easily found, and when any of the features mentioned above were seen

in one section of a lymph node, examination of multiple blocks was often necessary to find the worms.

Acute lymphangitis, epididymo-orchitis and acute funiculitis producing tender lumps in the course of the spermatic cord in the inguinal canal, were recognised. Chyluria, a well recognised complication, was encountered occasionally.

Microfilariae were sometimes found incidentally in tissue sections of various organs, e.g. lung and brain. Wilkey (1970) found microfilariae in the spleens of three patients on whom forensic autopsies were performed because they died suddenly and unexpectedly. In one of these, microfilariae were also present in glomerular capillaries. (Fig. 143). No other significant pathology was demonstrated in any of these cases. In the spleens, small areas of infarction were found in association with the microfilariae. Whether these lesions contributed to the sudden deaths could not be ascertained, but Wilkey postulated that they may have precipitated an acute anaphylactic reaction.

Fungal Infections

Actinomycosis

Skin lesions, in which the so-called "ray fungus" was identified in histological sections of biopsy material, were included under this heading. Clinically these lesions consisted of multiple cutaneous sinuses discharging pus. The adjacent tissue was thickened by a marked fibrous tissue reaction. When the foot was involved the lesion was referred to as "Madura foot". Untreated, there was a copious discharge of pus. (Fig. 144). After prolonged treatment with penicillin,

streptomycin and sulphones, the purulent exudate decreased and at least partial healing occurred. (Fig. 145). However, surgical excision of the affected area was frequently the treatment of choice. (Fig. 146).

Histologically, there was fibrosis with a variable chronic inflammatory cell infiltration together with scattered, focal collections of polymorphs-microabscesses. The "ray fungus" was almost invariably to be found at the centre of such "abscesses". The appearance of the actual fungus was variable in that some had thin filaments and others thick filaments with or without the presence of well formed clubs at the periphery of the filamentous hyphae. Presumably this was just an indication that a number of different species of fungus caused a similar clinico-pathological appearance.

This was the commonest form of "deep mycosis" encountered in the histopathological material. The anatomical sites of 25 lesions observed during 1966-67 are shown in Table 35, and lesions of the arm and back are illustrated in Fig. 147.

TABLE 35

Anatomical Sites of 25 Cases of Actinomycosis

Foot and/or ankle	9
Lower leg	4
Trunk (anterior or posterior)	4
Thigh	3
Arm and shoulder	3
Anal verge	1
Elbow	1
	25

The author encountered no case involving oral cavity, face, neck or abdomen either in the two years reviewed, or in 1962-63 when about the same number of lesions were seen. This was a little surprising in view of the fact that standard text-books (Lewis et al, 1958) quote the cervicofacial region as being the primary site of involvement in over 50% of cases, and the alimentary tract (appendix and liver) as being the next most common site.

Many species of fungus of the genera Actinomyces and Nocardia can cause this histological appearance. Unfortunately, facilities for mycological examination were very limited, and fungal cultures were not performed on any of these cases.

Superficial Mycoses

Tinea Imbricata involving usually the whole of the body surface (Fig. 148) was very common, especially among coastal peoples. A limited mycological survey of superficial mycoses was made in the author's laboratory in Port Moresby (Reid, 1966). Virtually the only species of Dermatophyte isolated from such cases was Trichophyton concentricum.

Tinea versicolor was also fairly common, and several members of the hospital staff in Port Moresby suffered from this.

Four cases of Chromoblastomycosis were diagnosed in Port Moresby during 1966-67. (Fig. 149). The diagnosis was confirmed by biopsy or fungal culture, or by both of these methods.

Tropical Ulcer

The so-called "tropical ulcer" refers to chronic ulceration, usually of the lower leg, which is commonly encountered in tropical countries. (Fig. 150 (a)). The ulcer presumably results from infection of an abrasion occasioned by walking through the thick, tropical undergrowth. Spirochaetes and fusiform bacilli can usually be identified in exudate scraped from the floor of the ulcer, but no specific causative agent has been recognised.

Repeated trauma causes continuation of the ulceration. When healing occurs it is usually accompanied by gross scarring. Fig. 150(b) illustrates scarring producing a band-like stricture of the lower leg. One specimen submitted to the author for histological examination was portion of a lower leg in which spontaneous amputation had occurred, possibly as a later manifestation of a process like this. The long-standing infection commonly produces marked periostitis in the underlying bone, and the scarred skin and slightly bowed tibia illustrated in Fig. 151 probably resulted from long-standing tropical ulcer. Malignant change is recognised as a further complication.

Tropical ulcers were very common in T.P.N.G. during the 1950's, but it was the impression of many doctors that they had become much less common during the 1960's. One possible explanation for this may be that first aid dressing of wounds, and penicillin injections were much more readily available in the villages during the latter decade. Even so, they still accounted for 3.5% of hospital admissions in the period 1963-1966. (Vines, 1970).

Donovanosis

This condition, also called granuloma inguinale, is a mildly infectious disease. It is probably caused by intracellular organisms which can be found in the cytoplasm of large histiocytes present in the purulent discharge from the lesions. It is spread by sexual contact and is fairly common in most countries in which the standard of hygiene is low. (Ratam and Rangiah, 1954).

Sporadic cases were diagnosed prior to 1964, but Maddocks (1967) drew attention to a relatively recent upsurge in the prevalence of this disease in Port Moresby. He found that it was second to gonorrhoea as a cause of venereal disease, and he described the clinical features, and the response to treatment.

The main clinical manifestations are illustrated in the accompanying photographs of patients examined by the author. (Figs. 152, 153, 154 & 155). The infection was nearly always confined to the ano-genital area, but disseminated lesions did occur. For example, the man shown in Fig. 156 had discharging sinuses from inguinal lymph nodes, and the woman shown in Fig. 157 had multiple discharging sinuses over the lower part of the anterior abdominal wall. In such disseminated cases, the organism-containing histiocytes were identified in smears of the pus obtained from the various sites.

When the technique of preparing smears from granulation tissue nipped off the lesion itself was introduced, the characteristic histiocytes (Fig. 154 (b)) were readily identified in Giemsa stained smears. The histological appearance of biopsy specimens was rather variable. (personal observation). There was usually some thickening

of the surface epithelium together with a variable degree of chronic inflammatory cell infiltration in the dermis. The foamy histiocytes with organisms in their cytoplasm were occasionally quite numerous, but more often than not they were scanty. Examination of smears, which in any case was simpler than biopsy, became the standard method of laboratory diagnosis in T.P.N.G.

Scrub Typhus

This Rickettsial disease was encountered in various parts of T.P.N.G. Fig. 162 shows an eschar on the leg of an Australian resident. Fig. 163 shows this patient's temperature chart, and the dramatic recovery which took place after treatment with Chloramphenicol. The author did not encounter any indigenous patients with this disease.

Rhinoscleroma

This is an infective condition characterised by the presence of granulation tissue in the nose and nasopharynx. It causes gross enlargement of the nose and blockage of both nostrils. (Fig. 164). The process may spread on to the skin of the face, and may extend further down the respiratory passages into the larynx and trachea, causing respiratory obstruction from which the patients ultimately die. Histologically the granulation tissue consists of masses of plasma cells through which foamy histiocytes can be found. These histiocytes are present in variable numbers (Fig. 165) and contain gram negative bacilli in their cytoplasm. The organisms are thought to be the cause of the condition and to belong to the genus Klebsiella.

Rhinoscleroma, which occurs in many parts of the world, is

relatively common in T.P.N.G., particularly in the Western Highlands. Cases with lesions in the nose, nasopharynx, larynx and trachea were seen by the author.

Tuberculosis

Tuberculosis was a very common and very important disease in T.P.N.G. From 1962-1966 it accounted for 6.4% of all hospital deaths. This was the third most common cause of death after pneumonia (25.5%) and gastroenteritis (7.5%) (Vines, 1970). It was also the principal cause of bed occupancy in the hospitals throughout the country - 31% of all beds occupied. 13% of patients being treated for tuberculosis were suffering from the glandular form of the disease.

During this period there were very few deaths from tuberculosis in the Highlands region. (Department of Public Health, Hospital Disease Statistics 1963-64, 1967). Early diagnostic surveys had established the almost complete absence of the disease from the Highlands, and vigorous efforts were made to minimise the possibility of introducing it. This involved careful screening of all labourers recruited from the Highlands for work in coastal areas. Before and after their contracted term of two years they were examined, and any who were found to be suffering from tuberculosis were treated before being repatriated. As almost all travel to the Highlands was by air before 1965, these preventive measures were fairly satisfactory. With the opening of a road link between the Highlands and the coastal town of Lae in 1965, easy and quick access to and fro became possible. Regrettably it must be expected that the prevalence of tuberculosis in the Highlands will increase in the coming years. (Wigley, 1967).

Material and Results

Among the 1,100 autopsies performed between 1962 and 1967 there were 80 cases of tuberculosis - 7.3% of all the autopsies. Only 7 of these came from the Highlands region, all before 1965.

The age and sex distribution of these cases is shown in Fig. 166.

The cases appeared to be fairly evenly distributed throughout all age groups and there was no significant difference in prevalence between the two sexes.

The morbid anatomical details were rather meagre in many of the post mortems performed outside Port Moresby. However, the following patterns were reported in the post mortem protocols. (Table 36).

TABLE 36

Organs Involved in 80 Tuberculosis Post Mortems

Disseminated tuberculosis	35
Exact organ distribution not specified	20
Pulmonary involvement only	8
Meningitis the main cause of death	6
Pericarditis the main cause of death	5
Tuberculoma of the brain	2
Abdominal organs only involved	2
Pulmonary tuberculosis an incidental finding	2
	80

In cases of disseminated tuberculosis there were miliary "tubercles" throughout most organs, particularly the liver, spleen, lymph nodes and kidney. The tubercles could be recognised as tiny yellow or creamy spots beneath the capsule, or on the cut surface of the organs. Histologically the majority of these showed the "classical" features of tubercles with epithelioid cells, Langhan's type giant cells and centralcaseation, but they frequently consisted only of focal areas of necrosis with little cellular reaction, or sometimes mainly a polymorphonuclear one. Acid fast bacilli were frequently present in large numbers in such lesions.

The majority of patients being treated for tuberculosis had pulmonary manifestations, and this pattern was also present in the autopsies. The lungs were involved in most cases of disseminated tuberculosis and also in most of the cases in which the exact organ distribution was not specified.

The pulmonary manifestations were variable. In some there was a true "miliary" distribution with tiny yellow or creamy coloured tubercles scattered diffusely and evenly throughout both lungs. In others there was a tuberculous pneumonia, sometimes with cavitation. (Fig. 167). Empyemas were noted in a few cases. Mediastinal lymph nodes were frequently involved. Calcified "primary foci" were found incidentally in a number of lungs which showed no other evidence of tuberculosis. Grossly scarred or calcified areas suggesting spontaneous healing were not found in any post mortem lungs. Some lungs removed at thoracic surgery were grossly scarred and showed no evidence of active tuberculosis. (Fig. 168). These patients had been receiving drug therapy for some years prior to surgery.

Meningitis was the main cause of death in 6 cases, being part of a generalised infection including the lungs in 4 of these.

Acute pericarditis was the main finding in 5 cases. Again, almost all of these were accompanied by tuberculosis of other organs. A few cases of chronic constrictive pericarditis were seen during life, but examination of the pericardiectomy specimens showed no evidence of active disease.

Abdominal tuberculosis

One of the two post mortem cases had the well documented features of the gastrointestinal disease with multiple areas of mucosal ulceration throughout the small intestine, marked thickening of the ileocaecal valve region, involvement of the appendix, and ulcers of the colon extending to the mid-transverse colon. (Figs. 169 & 171 (b)).

Tubercles were visible through the serosa of the bowel wall, and the mesenteric lymph nodes were grossly enlarged. (Fig. 170). The other patient, a young adult male, was more difficult to diagnose. He had obstructive jaundice, and at post mortem a large, creamy necrotic mass was found in the pancreas. Similar masses were present in both lobes of the liver. The doctor who performed the post mortem examination thought this was a carcinoma of the pancreas with hepatic secondaries. Histologically these consisted of masses of necrotic material associated with a light infiltration of polymorphs and teeming with acid fast bacilli.

Examples of various forms of abdominal tuberculosis were also encountered in the surgical pathological material. For a short

period during 1962 a number of surgeons independently began performing laparotomies on patients presenting with ascites. Many of these had cirrhosis, but at least one third of them had miliary "tubercles" spread throughout the peritoneum. Before biopsy confirmed the nature of these lesions, they were almost indistinguishable from deposits of secondary neoplasm. Chest x-rays performed on many of these patients showed no evidence of pulmonary tuberculosis. Occasionally, cases of chylous ascites were observed. A few hernial sacs submitted for histological examination at the time of inguinal herniorrhaphy showed miliary "tubercles". In such cases the development of tuberculous ascites may have been the cause of the hernia.

The tuberculous process occasionally involved a localised area of the alimentary canal. The caecum and ascending colon illustrated in Fig. 171 (a) was removed because of a mistaken diagnosis of carcinoma of the caecum. When opened longitudinally, tell-tale "tubercles" were clearly visible in the thickened colonic wall. The appendix was often involved as part of generalised intestinal tuberculosis, but an occasional one was submitted for histological examination after a "routine" appendicectomy.

Glandular Tuberculosis

As indicated above, 13% of tuberculosis patients had this form of the disease. Lymph node biopsies for diagnosis of T.B. were to the surgical pathologist in T.P.N.G. what appendicectomies are to the surgical pathologist in Australia.

The cervical lymph nodes were the ones most commonly affected. Clinically the nodes felt rubbery and rather matted. They sometimes

connected with sinuses discharging on the skin surface. (Fig. 172). When cut, yellow or creamy "tubercles" could be seen on the cut surface. Histologically the commonest pattern consisted in the usual appearance of tuberculous granulation tissue with collections of epithelioid cells around a central area of caseation. Sometimes, only masses of necrotic "caseous" material could be found in the node with virtually no epithelioid cells or giant cells. At other times the node was studded with focal collections of epithelioid cells with a few multinucleated giant cells, but without any evidence of caseation. Eosinophils in large numbers were seen in some cases. Acid fast bacilli were usually absent or very difficult to find.

Interpretation of these various histological patterns was sometimes difficult. In some, the appearance was identical to that seen in cat scratch disease; in others it resembled sarcoidosis; while in a small number, only necrotic material was obtained on biopsy. In some children, cervical lymphadenopathy was so gross as to be on the point of causing death from asphyxiation. The clinical diagnosis in such cases lay between tuberculosis and malignant lymphoma, and histological diagnosis was crucial. The response to antituberculous therapy when this was the correct diagnosis, was quite spectacular, with relief of the respiratory obstruction occurring within a day or two of the commencement of therapy.

B.C.G. Lymphadenitis

Quite a few axillary lymph nodes which had suppurated and produced discharging sinuses following B.C.G. vaccination were submitted for histological examination. These had a similar appearance

histologically to that seen in true tuberculous lymph nodes.

Other Forms of Tuberculosis

No case of bone or joint tuberculosis appeared in the post mortem series, but they are discussed in Chapter 12. Tuberculosis of the central nervous system is discussed in Chapter 13. Hepatic tuberculosis is discussed in Chapter 7.

Amyloidosis

At the time of death, 7 of the 80 patients (9%) were found to have histological evidence of amyloidosis.

Bacteriology

The human variety of Mycobacterium tuberculosis was isolated from the sputum of numerous patients and from a few post mortem lesions. Sensitivity tests were performed on a small number of organisms, but too few had been done by the end of 1967 for any particular pattern to be noted.

Discussion

Backhouse (1956) reported his experience of the morbid anatomical features of tuberculosis encountered in 1,541 post mortems performed in Rabaul between 1922 and 1940. His material did not include surgical specimens, but there appears to have been little change in the morbid anatomical features of the disease during the intervening period. Both reviews demonstrated the absence of cases

of fibro-caseous tuberculosis, the presence of large numbers of patients with tuberculous lymphadenopathy, and the presence of large amounts of caseation in the lesions.

The evidence available indicated that the infecting organism was a human strain of M. tuberculosis, and that transmission of the disease was by person to person contact. Although most parts of T.P.N.G. were sparsely populated, the people crowded into small, poorly ventilated huts each night, and this made transmission of the disease easy. Milk was not drunk anywhere in the country, so transmission by this means could be discounted.

The histological appearances of many of the tuberculous lymph nodes resembled closely those described by Campbell (1969) as being caused by "anonymous" mycobacteria. An adequate bacteriological examination of such lymph nodes has not yet been undertaken to clarify this possibility.

The prevalence of amyloidosis (9%) was high when compared with the prevalence of 1% among post mortem cases of tuberculosis seen in London in the pre-antibiotic years 1908-1910. (Turnbull, 1914). (see Chapter 2).

Summary

The pathological features of tuberculosis in T.P.N.G. have been presented. This was an important disease because of its prevalence, and the proportion of the hospital beds occupied by patients suffering from it.

Diagnostic difficulties encountered included the differentiation of a tuberculoma from a neoplasm of the caecum, liver and brain; the differentiation of peritoneal "tubercles" from disseminated malignancy; and the histological diagnosis of tuberculosis when there were large amounts of caseation and minimal cellular reaction, and when, particularly in lymph nodes, there were "tubercles" without any evidence of caseation.

For a further understanding of the pathology of this disease as it occurs in T.P.N.G., it is suggested that two lines of investigation might be undertaken.

(1) More detailed bacteriological examinations of the causative organism - including its type, its virulence, its antibiotic sensitivity patterns, and to what extent "anonymous" mycobacteria are involved.

(2) The reaction of the population to this disease in relation to the absence of fibro-caseous pulmonary tuberculosis, the high prevalence of amyloidosis, and the unusual reaction to Mantoux tests as reported by Wigley (1967).

Mycobacterium Ulcerans

Skin ulceration caused by M. ulcerans has been recognised in T.P.N.G. for some years. The epidemiology of the disease throughout T.P.N.G. has not been fully documented. However, the author examined biopsies from cases from many parts of the country, and Reid (1967) described the clinical features and surgical management of cases from the Kamusi River area near Popondetta on the north coast.

Over half of Reid's cases were children. The ulcers occurred most commonly on the limbs, but the trunk could also be affected. The sex incidence was equal.

Characteristically there was a small area of skin ulceration, but the skin around the obvious ulcer was greatly undermined. The area of necrosis usually involved only the subcutaneous tissue, but in a few cases the underlying muscle was also involved. By lifting the edge of the ulcer a probe could be passed well under the skin in all directions. The rate of extension of the area of ulceration was variable. Sometimes it spread with amazing rapidity while at other times extension took weeks or months. Left untreated, healing occurred slowly, and when the ulceration involved the skin over a joint, gross contractures occurred.

For purposes of bacteriological diagnosis it was important to obtain some of the necrotic, subcutaneous tissue from the advancing edge of the ulcer. In treatment also, it was necessary to identify the advancing edge so that the lesion could be completely excised and the area skin grafted.

Histologically there was some variability in the appearances of these lesions. (personal observation). In acute cases there was a moderate degree of chronic inflammatory cell infiltration in the dermis with necrotic, relatively acellular material at the dermo-subcutaneous junction. Acid fast bacilli, often in large numbers, were usually present. Sometimes however, no organisms could be found. In other cases, presumably of longer duration, there was a heavy chronic inflammatory cell infiltration in the dermis together with focal

collections of epithelioid cells and a few multinucleated giant cells. Acid fast bacilli were found infrequently in such sections, and culture of the organism was necessary for a definite diagnosis to be made.

CHAPTER 10

GOITRE

Endemic goitre (Fig. 173) was prevalent in most parts of T.P.N.G. Goitre surveys were carried out by McCullagh (1963) and later by Buttfield (1965). These demonstrated that the prevalence of goitre, as measured by the visible goitre rate, increased with altitude, and that the majority of the goitres were in young adult females. They confirmed that these goitres were due to iodine deficiency which could be corrected by intramuscular injections of iodised oil. Buttfield postulated that the goitres were a manifestation of failure of adaptation of the people to iodine deficiency.

During 1962 and 1963 many goitres were submitted for histological examination. A number of these were similar to goitres seen in Australia, but there was a significant proportion which were extremely hyperplastic, and in which there was confusion as to whether they should be labelled benign hyperplastic, or neoplastic goitres. The appearances seen in these endemic goitres seemed to be different from those described in the authoritative dissertation on the pathology of endemic goitre by De Smet (1960). It was decided therefore to undertake a study of the pathology of the goitres submitted for histological examination during 1966-67. Fewer thyroidectomies were performed in this period than in the 1962-63 period because the surgeons had been impressed by the dramatic response of most goitre patients to the intramuscular injections of iodised oil. Virtually all the thyroids removed throughout T.P.N.G. during this two year period were submitted for histological examination.

Material

During 1966-67, 76 thyroids were submitted for histological examination. Photographs were taken of many of these specimens, and multiple blocks were taken from each one. Detailed notes of the pathological features were kept prospectively, and unstained sections from the hyperplastic glands were kept for study at a later date. These were subsequently stained and reviewed.

Results

The diagnoses made on the 76 thyroidectomy specimens examined during 1966-67 are shown in Table 37.

TABLE 37

Pathology of 76 Thyroidectomies 1966-67

	No.	Unilateral	Bilateral
Adenomatous hyperplasia	33	16	17
Colloid goitre	25	13	12
Mixed adenomatous hyperplasia and colloid goitre	6	3	3
Amyloid goitre	2		
Thyroid carcinoma	10		
	76		

Age and Sex Distribution

The age and sex distribution of the 66 cases of benign goitre is shown in Fig. 174. The male to female ratio was 1 to 3 and the

majority were in the age range 11-30 years.

Pathology

The glands labelled adenomatous hyperplasia were soft and rubbery. On their cut surface they showed one or more well circumscribed soft, creamy, homogeneous nodules varying in size from 1 to 4 cms. in diameter. The thyroid tissue adjacent to the nodules retained a normal lobular pattern in which glistening colloid could be seen. (Figs. 175 & 176). The gland illustrated in Fig. 177 showed a mixed pattern of adenomatous hyperplasia and colloid goitre. Histologically the nodules were composed of thyroid acinar cells which were greatly enlarged, with hyperchromatic nuclei. These cells were arranged in sheets with small acini scattered among these relatively undifferentiated areas. The acini contained very little colloid. 11 of the hyperplastic nodules were not surrounded by a fibrous tissue capsule and there was an abrupt edge to the nodule. This was surrounded by rather compressed, but normal looking thyroid acini. (Fig. 178). In 22 cases the nodules were surrounded by a thin capsule of fibrous tissue which separated them from the adjacent, normal looking thyroid tissue. There was very little fibrous tissue through the adenomatous nodules. A few of them contained small scattered areas of calcification.

The colloid goitres showed a diffuse change throughout the gland with dilatation of most of the thyroid acini. (Fig. 179). These acini were filled with colloid, and the epithelial cells of the follicles were flattened and small. Many of the acini had undergone cystic dilatation, and in a few cases the thyroid enlargement was due to a single colloid cyst. (Fig. 180). The stroma of such glands

showed varying degrees of hyalinisation, fibrosis and haemorrhage. Calcification was commonly seen in the stroma. Occasionally this was extensive, giving rise to a rock hard goitre. These glands contained no histologically normal thyroid tissue.

Half the thyroidectomies were for unilateral enlargement of the thyroid and half were for bilateral enlargement.

The two amyloid goitres were submitted with a clinical diagnosis of carcinoma or Riedel's struma. Further clinical enquiry revealed that both of these patients had primary amyloidosis and this topic was dealt with in Chapter 2.

Of the 10 carcinomas, 6 were papillary and 4 were follicular. The details of their presentation are shown in Table 38.

TABLE 38

Thyroid Carcinomas 1966-67

Presentation	No. Cases
Metastases in cervical lymph nodes	5
Thyroid enlargement	
Marked ulceration of the overlying skin	1
A well-circumscribed nodule of papillary carcinoma	1
Follicular carcinoma of the thyroid with secondaries in cervical lymph nodes	1
Bone secondaries	2
	10

Seven of these were females and two were males. No sex was recorded on the histology request form in one case.

Discussion

Goitres showing the features described as adenomatous hyperplasia were the commonest type encountered in thyroidectomy specimens in T.P.N.G. This type of goitre was not featured in the review of the pathology of endemic goitre by De Smet (1960), whose material was drawn from areas of endemic goitre throughout the world. Buttfield (1965) showed that most of the features of endemic goitre in T.P.N.G. resembled those encountered in other endemic areas. One way in which they differed, however, was that the protein bound iodine levels of goitrous people in T.P.N.G. were in the hypothyroid range, indicating that this population was probably more severely iodine deficient than any other population previously investigated.

The adenomatous hyperplasia may be due at least partly to the severe iodine deficiency. However these goitres resembled the histological appearance seen in dyshormogenetic goitre, (Williams, 1966); and therefore a deficiency in one of the enzymes involved in the synthesis of thyroxin cannot be entirely overlooked. Marine and Lenhart (1909) demonstrated that the thyroid glands of dogs given iodine deficient diets developed nodular hyperplasia, which histologically resembled the appearances seen in these hyperplastic goitres in T.P.N.G. They showed that if iodine was replaced in physiological doses, a colloid goitre was produced. However, if larger doses of iodine were given, the enlarged gland returned to normal. In view of this it may be postulated that those patients with colloid goitres may have come from

areas close to centres where imported food was available. This may have contained small amounts of iodine. Those with adenomatous hyperplasia on the other hand, may have been restricted to naturally available food. Unfortunately the data did not allow such deductions to be made, because the precise location of patients' dwellings, and their dietary habits were not recorded.

Buttfield demonstrated a significant decrease in goitre size in 60 of 61 patients three months after an injection of iodised poppy seed oil (Neo-hydriol). In these 60, a change was visible both to the patients themselves, and to the observers. In 32 of the 60, the change was quite significant, the goitres decreasing from size 2 to size 1 or 0, i.e. visible to invisible.

Comparing the results of the pathological examination of goitres treated by thyroidectomy, and the results obtained from therapy with intramuscular iodised oil, it can be postulated that:

1. Those goitres which demonstrated a significant and dramatic reduction in size 3 months after treatment were predominantly of the adenomatous hyperplasia type - 32 of the 61 patients treated, compared with 33 of the 64 goitres submitted for pathological examination.

2. Those goitres which demonstrated a less rapid response to treatment were probably of the colloid type.

It is well known that the goitre rate in areas of endemic goitre can be reduced by increasing the dietary intake of iodine; but treatment of individual patients with colloid goitre produces very little change in the size of the thyroid gland. Those glands in which

large amounts of calcification were present would not be expected to respond to any therapy. Neither would amyloid goitres be expected to respond to iodine therapy.

Buttfield accepted that the rapid return to normal size of half of his series of enlarged glands was due to the return to normal size of grossly hyperplastic glands. He suggested that the partial regression of the remaining ones was due to the presence of fibrous tissue in the glands. In view of the paucity of fibrous tissue in the hyperplastic glands examined by the author, this explanation seems less likely than the one postulated above.

Buttfield noted the prevalence of unilateral enlargement of the thyroid glands and this was also observed in the pathological material. He was however, unable to explain this in the light of his finding of raised T.S.H. levels in patients with goitre.

Malignant tumours of the thyroid accounted for 2.1% of all tumours reported to the tumour registry. This did not appear to be an exceptionally high prevalence. Buttfield (1965) did not encounter a single case of thyroid carcinoma in his field surveys, and this further supports the view that the prevalence of thyroid carcinoma was not unduly high in this population. Surveys conducted in other areas in which endemic goitre is prevalent have likewise not revealed any increased prevalence of thyroid cancer in such populations.

Twenty-three of the 49 thyroid carcinomas notified to the tumour registry from 1958-1967 were recorded as being follicular carcinomas. In most published series (Anderson, 1961), papillary carcinomas were the commonest type encountered. In the small series in 1966-67

this was also the case. Review of some of the tumours which had been labelled follicular carcinoma revealed features which the author would have classified as adenomatous hyperplasia. In view of the difficulties in interpretation of the histological appearances of these nodules, caution should be exercised when calling them carcinomas. A diagnosis of follicular carcinoma should probably be made with certainty only when evidence of local invasion or distant metastasis is present.

Summary

The pathological features of benign goitres in T.P.N.G. have been described. Half of these goitres demonstrated features of adenomatous hyperplasia which was more striking than in other populations in which endemic goitre was prevalent. It was postulated that this form of goitre was due to extreme iodine deficiency. It was further postulated that those goitres which were shown in field trials to respond dramatically to treatment by intramuscular injections of iodised oil were of this type.

The difficulties in interpreting the histological appearances of these goitres were mentioned. Unless definite evidence of malignancy, such as invasion of vessels or distant metastasis was demonstrated, such goitres should be regarded as being benign. Because of the response to iodine therapy in approximately 50% of patients with goitres, surgeons were inclined to prescribe a trial of iodine therapy before contemplating surgical treatment for the majority of goitres.

CHAPTER 11

CARDIOVASCULAR SYSTEM

Cardiovascular disease was relatively uncommon during the period of this review, accounting for only 0.2% of all hospital admissions throughout the country. "Department of Public Health Hospital Disease Statistics, 1963-64", (1967). A small number of reports of cardiovascular disease in T.P.N.G. have been published. Campbell and Arthur (1964) found that 0.9% of 2,000 admissions to the adult medical ward of the Port Moresby General Hospital were cases of cardiovascular disease. There were 13 cases of cor pulmonale, which was the commonest cause of heart failure in these patients, and 8 cases of chronic rheumatic carditis. Korner (1964) after a two months visit to Lae, reported 15 cases of cardiac disease which he had observed in the hospitals in Lae, Wewak, Madang, Mt. Hagen and Goroka. His diagnoses were as follows:

	No. Cases
Cor pulmonale	3
Cardiomyopathy	3
Rheumatic heart disease	3
Congenital heart disease	1
Constrictive pericarditis	1
Myocarditis associated with sepsis & anaemia	1
Cardiomegaly due to anaemia	1

Kariks and McGovern (1967) reported 29 cases of cardiac disease in 167 consecutive post mortems performed in Rabaul. 8 of

these had amyloid deposits in the heart as part of a generalised primary amyloidosis. A further case with sub-acute bacterial endocarditis also had amyloid deposits in the myocardium. There was one case of mitral stenosis, and 19 cases of interstitial myocarditis. All except one of these latter cases were mild, with only patchy infiltrations of lymphocytes. In only one case, a five year old child, was any necrosis of myocardial fibres seen. Vines (1970) in his epidemiological sample survey found only a handful of cases of heart disease in his examination of 3,000 patients throughout the country. These included 1 patient with congenital heart disease, one with aortic stenosis, and a small number with chronic cor pulmonale and congestive cardiac failure associated with pneumonia and pregnancy. He did not encounter any patient with chronic rheumatic heart disease. Hypertension, except as a complication of chronic renal disease, was extremely rare.

Backhouse (1958) reported 12 cases of atheroma in a series of 724 post mortems performed in Rabaul between 1923 and 1934. It would appear from his descriptions that at least 7 of these were probable cases of Takayasu's arteritis. He found no case of myocardial infarction. In only one post mortem was even moderate narrowing of the lumena of the coronary arteries noted. This post mortem series was somewhat selected because 93% of the cases were males and 80% of them were aged between 15 and 30 years.

Magarey et al (1969) reported the results of a survey of atherosclerosis in T.P.N.G. Aortas were removed from 217 consecutive post mortems performed in Rabaul and Port Moresby. (The 55 aortas from Port Moresby were submitted by the author). These were matched for

comparison with aortas removed at post mortem from Australian patients in Sydney. It was found that the prevalence and severity of this condition were less than had been reported in any previously investigated population group. Cooke and Kariks (1970) reported their combined experience of myocardial infarction in a total of 995 post mortems performed between 1962 and 1968. There were 8 cases, which further emphasised the rarity of this form of cardiovascular disease which is so prevalent in the technologically advanced countries of the world.

What follows is an account of the author's experience of cardiovascular disease.

Material

For the purpose of this analysis, only material personally handled by the author has been included. This consisted in 640 post mortems performed during the 4 years 1962-63 and 1966-67. Approximately half of these were performed by the author in Port Moresby, and the rest by doctors working in the out-lying centres. Blocks of tissue from the latter were submitted to Port Moresby for histological examination. Post mortems performed on neonates up to one month of age and on expatriates were excluded. The aortitis which resembled Takayasu's arteritis is dealt with separately.

Cardiac Conditions Other Than Aortitis

The cardiac conditions encountered in the post mortems are shown in Table 39.

TABLE 39

Cardiac Conditions in 640 Post Mortems

Old rheumatic carditis	
Aortic valve alone	6
Mitral valve alone	4
Both valves	2
Cor pulmonale	9
Bacterial endocarditis	
Aortic valve alone	2
Affected valve not specified	5
Myocardial infarction	6
Acute myocarditis	4
Acute pericarditis	
Tuberculous	2
Other	1
Acute rheumatic fever	2
Hypertensive heart disease complicating chronic pyelonephritis	1
Idiopathic left ventricular hypertrophy	1
	45

Other forms of cardiovascular disease which were encountered included the following:

1. 7.3% of all the autopsies showed evidence of amyloidosis. As indicated in Chapter 2, approximately 90% of these had at least small deposits of amyloid in the vessels and interstitial tissue of the heart. Some of them were recorded as having clinical signs attributable to the

amyloid.

2. Four congenital hearts were observed in the neonatal autopsies. (Chapter 17).

3. Two patients, both males approximately 50 years of age, died from acute cerebral infarction due to recent thrombosis of the middle cerebral arteries. (One was a left-sided infarct and the other a right-sided one). A further patient, a male aged 40 years died as a result of an intracerebral haemorrhage in the region of the internal capsule.

Comments

Old rheumatic carditis

These cases were diagnosed on the presence of stenosed and calcified valves. Hence the diagnosis was not proven conclusively in all of them.

Cor pulmonale

This diagnosis was made when right ventricular hypertrophy was present together with signs of right ventricular failure. Evidence of chronic pulmonary disease was present in most of these cases.

Bacterial endocarditis

Some of these were cases of acute endocarditis affecting what appeared to be previously healthy valves, while others were superimposed on valves which had previously been affected by rheumatic carditis. No

meaningful bacteriological results were available on these cases.

Myocardial infarction

The details of the six cases of myocardial infarction are listed in Table 40. They were all males, all relatively young by Australian standards, and they were born in a number of widely separated localities. No case was encountered in the relatively small group of the educated élite, most of whom were still below 30 years of age.

TABLE 40

Details of 6 Cases of Myocardial Infarction

Case No.	Sex	Age	District of Birth	Occupation	Mode of Death	Pathology
1	M	42	Highlands	Subsistence farmer.	Sudden death immediately preceded by acute abdominal pain.	Recent thrombus occluding anterior descending branch left coronary artery. No histological abnormality.
2	M	50	South coast	Labourer in Port Moresby.	Sudden death while working.	Atherosclerotic plaque almost completely occluding the origins of the circumflex and anterior descending branches of the left coronary artery. Moderate fibrosis in left ventricular myocardium. No recent infarction.
3	M	33	North coast	Plantation labourer.	Found dead in bed one morning.	Recent thrombus occluding anterior descending branch left coronary artery. Mild fibrosis in left ventricular myocardium. No recent infarction.

TABLE 40 (continued)

Case No.	Sex	Age	District of Birth	Occupation	Mode of Death	Pathology
4	M	40	South coast	Labourer in Port Moresby.	Sudden death preceded by chest pain of a few hours duration.	Recent thrombus occluding anterior descending branch left coronary artery. Recent anterior myocardial infarction demonstrated histologically.
5	M	36	South coast	Domestic servant for 10 years.	Sudden death 6 hours after onset of acute abdominal pain and vomiting.	Marked atherosclerosis of anterior descending and circumflex branches of left coronary artery with almost complete occlusion of the former. Minimal atherosclerosis of right coronary artery. No recent thrombus and no histological abnormality.
6	M	38	South coast	Labourer.	Diagnosed on clinical and electrocardiographic evidence as having an acute myocardial infarction in June 1966. Died suddenly and unexpectedly in November 1966.	Old anterior and posterior myocardial infarctions with fibrosis and thinning of the myocardium at these sites. (Fig.181). Marked atherosclerosis of the right coronary and the anterior descending branch of the left coronary arteries. No recent thrombus and no histological evidence of recent myocardial infarction.

Acute myocarditis

All four of these patients exhibited in many areas of the heart heavy focal infiltrations of mononuclear inflammatory cells associated with necrosis of myocardial fibres. They all died suddenly and unexpectedly. In all except one case, the condition was discovered on routine histological examination of the heart. The fourth case, a male aged 18 years, who died suddenly while playing football, had a lesion visible macroscopically. There was a rounded, haemorrhagic area 4 x 1.5 cms. beneath the epicardium on the posterior surface of the left ventricle, approximately 2 cms. distal to the mitral valve ring. The coronary arteries were patent and free of atheroma.

The patients all came from different parts of the country. There were two males, aged 18 and 60 years, and two females aged 1½ and 35 years respectively.

Acute rheumatic carditis

Two patients, a male aged 26 and a female aged 12 years, showed acute rheumatic carditis with numerous Aschoff nodules present through the myocardium.

Idiopathic left ventricular hypertrophy

This patient, a male aged 24 years died suddenly one evening in Port Moresby while talking to his friends. There was no history of previous illness. The only abnormality was a grossly enlarged heart which weighed 800 gms. The increase in size was due entirely to a gross concentric hypertrophy of the left ventricle which was 20 mms. thick at

the conus. (Fig. 182). All valves were normal. The foramen ovale was closed. The coronary arteries showed no atheroma and their lumena were patent. There was no coarctation, patent ductus arteriosus or any other aortic abnormality. The kidneys were both normal. Histological examination of the heart revealed gross hypertrophy of individual muscle fibres. There were small, focal collections of lymphocytes throughout the myocardium. No other abnormality was noted in any of the other organs.

A diagnosis of idiopathic left ventricular hypertrophy with small focal areas of myocarditis was made.

Discussion

Chronic rheumatic carditis was the commonest form of heart disease encountered in this post mortem series. Although only a few such cases were reported previously, many must have been occurring unrecognised in the general population. Apropos of this it was interesting to note the large number of patients with cardiac disease (mainly congenital and chronic rheumatic) who could be assembled in any regional hospital in the country, when teams of cardiologists visited T.P.N.G. to see whether such patients would benefit from cardiac surgery. (personal observation).

The importance of cor pulmonale as a cause of heart disease was reiterated in this survey.

Conditions such as bacterial endocarditis, myocarditis and pericarditis, were represented in this series, but no special features were noted.

Hypertensive heart disease was a rare condition.

One case of idiopathic left ventricular hypertrophy was observed. This condition is said to occur with relative frequency in Africa. (Edington and Gilles, 1969).

No case of thrombo-phlebitis was encountered by the author. This condition appeared to be relatively common in some parts of Africa. (Trowell, 1960).

Six cases of myocardial infarction were encountered. This was a relatively rare form of cardiac disease, and was certainly much more rare in the population of T.P.N.G. than in people living in the technologically advanced countries of the world.

Numerous factors are thought to play a part in the causation of coronary occlusion and myocardial infarction. Many of these were discussed in a review by Hipsley and Furnass (1966) in relation to the prevalence of coronary heart disease in Australia. Three factors which have received particular attention have been:

1. The decrease in physical exertion resulting from the revolution in mechanisation in the home, in transport and at work.

2. The increase in cigarette smoking.

3. The dietary intake of fat, particularly animal fat.

When the populations of countries such as Australia, and that of T.P.N.G. are compared with respect to these three factors, marked differences are apparent.

Hipsley and Kirk (1965) found that the energy expended each day by Papuans and New Guineans was comparable with that of Scottish clerks. The energy expenditure of the former, however, was more constant and regular through the day, and it was postulated that the difference in pattern of energy expenditure may be more important than the absolute value.

Detailed surveys of smoking habits in T.P.N.G. have not been undertaken, but casual observation indicated that the smoking habit was widespread, the material smoked being grown in the smoker's garden, and the quantity smoked probably being quite small. Until recently the one ounce of tobacco included in the weekly government ration was considered by the indigenous labourers to be an adequate amount. Since the establishment of a cigarette factory in Madang in 1963, the consumption of "tailor-made" cigarettes has increased greatly.

A number of dietary surveys have been undertaken throughout T.P.N.G. (De Wolfe and Whyte, 1958; and Bailey, 1963). These revealed that the dietary intake of fat was very low, and was mostly of vegetable origin. Associated with this was the fact that serum cholesterol levels examined in many population groups throughout the country ranged between 120 and 190 mgs.%. (personal observation).

As the development of T.P.N.G. progresses, rapid and profound changes will take place in the environmental conditions and patterns of life of the people. These changes might result in an increase in the prevalence of myocardial infarction, so that it approaches the importance it has in the industrialised countries of the world.

As indicated in Chapter 2, amyloidosis is unusually prevalent

in T.P.N.G. and this may have been responsible for some of the "cardio-myopathies" reported by Korner (1964).

In view of the low prevalence of atherosclerosis and of hypertension, it was not surprising that only 3 cases of cerebrovascular accident were encountered.

Summary

A review of the author's experience of cardiovascular disease other than aortitis has been presented. This constitutes the most comprehensive account of this form of disease as it occurred in T.P.N.G. during the period under consideration.

Aortitis

In 1908 the Japanese opthalmologist Takayasu reported the case of a 21 year old girl with cataracts and abnormal anastomoses between the retinal arteries and veins. Since then an extensive literature has accumulated on a form of arteritis which has come to be called Takayasu's arteritis. The clinico-pathological features of this condition were summarised in a recent review. (Hachiya, 1970). It consists in a form of arteritis of undetermined aetiology that affects the aorta, the proximal portions of its major branches, and the pulmonary arteries. It can produce stenosis, occlusion, dilatation or aneurysm. It has been recognised under a variety of different names in all countries of the world. It is relatively common in Africa (Isaccson, 1961; Schrire and Asherson, 1964) but is most prevalent in Japan, Korea and other parts of South East Asia. It affects both sexes, but particularly young women. The age range of reported cases has been from 3 to 66 years, with a mean of 26 years in women and 31 years in men.

The symptoms are usually related to the site of the vascular occlusion. Inadequate carotid circulation causes vertigo, syncope, headache and visual disturbances. Absent or diminished pulses in the neck or extremities, and claudication of the arm are due to occlusive changes in the proximal portions of the vessels to these areas. Vascular murmurs are often audible over the stenotic arteries. Hypertension is often present and is due either to stenosis of the renal arteries or to the coarctation-like narrowing of the lumen of the aorta. Aortic insufficiency is not uncommon as a late complication of the disease and is secondary to dilatation of the ascending aorta. Death may occur from complications of the hypertension or from rupture

of an aortic aneurysm.

Aortitis closely resembling the features described in Takayasu's arteritis was recognised by the author in the post mortem material in T.P.N.G., and the following account is based on the observations made on 14 such cases.

Material

Cases 1 to 8 were from the author's own post mortem series. Cases 9, 10 and 11 were from post mortems performed in Rabaul by Dr. J. Kariks. Case 12 was a post mortem performed by Dr. I. Wilkey in Port Moresby. Case 13 was a patient of Dr. C. Matthews in Lae, where he also performed the post mortem. Material from this post mortem was referred to the author by Dr. I. Wilkey. Case 14 was a patient of Dr. M. Murphy of Brisbane, and the aortogram was performed on this patient at the author's suggestion by Dr. S. Moro at the Royal Brisbane Hospital.

Results

Table 41 shows the age and sex distribution of these 14 cases, the region in which they were living, and the portions of the aorta and its main branches which were involved.

There were 8 males and 4 females, while in two cases the age and sex were not recorded. The ages ranged from 15 months to 53 years. Most were young adults. Cases came from the south coast, north coast and islands regions. There were none from the Highlands.

Case No.	Sex	Age	Region*	Aortic Arch Involved	Thoracic Aneurysm Present	Thickening and Stenosis of Aortic Arch Vessels	Whole Aorta Involved
1	F	29	N.C.	+	-	+	+
2	M	20	N.C.	+	-	?	?
3	M	40	N.C.	+	+	-	?
4	-	-	I.	+	+	?	?
5	-	-	I.	+	+	?	?
6	M	26	S.C.	+	-	+	+
7	F	40	S.C.	+	-	-	+
8	F	15 mths.	I.	+	-	+	+
9	M	53	I.	+	+	-	-
10	M	40	I.	+	+	+	-
11	M	30	I.	+	+	-	-
12	M	25	S.C.	+	-	-	-
13	M	30	N.C.	+	+	-	?
14	F	28	S.C.	+	+	-	+

* N.C. north coast

S.C. south coast

I. islands

The aortic arch was involved in all. The arch alone was involved in 4, the whole aorta in 5, and the thoracic aorta only was examined in a further 5. There was thickening and stenosis of the aortic arch vessels present in four, and absent in six of the ten in which this was specifically recorded. Thoracic aneurysm was present in six cases. In case 14 there were multiple aneurysms in the aortic arch, abdominal aorta and renal arteries.

From the data available, the prevalence of this condition in the population could not be accurately assessed. This information should emerge as the clinico-pathological features become more widely known, and more cases are diagnosed.

Clinico-Pathological Features

Case 1. A 29 year old female nurse whose radial pulses were not palpable. She had borne two children, the last, two months before she suddenly developed symptoms and signs of a subarachnoid haemorrhage. She died two days later. The brain, heart and aorta were fixed and then submitted for examination.

The cause of death was a subarachnoid haemorrhage from rupture of an aneurysm at the bifurcation of the right middle cerebral artery. Unfortunately, no histological section was taken from this artery. The heart appeared normal in size. The lumen of the anterior descending branch of the left coronary artery was reduced by approximately one-third of its normal diameter. The right coronary artery showed a small amount of atheroma. The myocardium appeared normal. The aortic valves were normal, and for approximately 5 cms. distal to the aortic valve, the aorta was relatively soft and pliable. Beyond

this point and extending to the bifurcation, the aortic wall was thickened and calcified, forming a fairly rigid tube. The lumen was irregular due to the presence of large numbers of atheromatous plaques on the intimal surface. There were also numerous small dilatations throughout the length of the aorta. The wall of the innominate, left common carotid and left subclavian arteries were also calcified in their proximal extent, and their lumena were almost completely occluded by atheromatous plaques. There were some small aneurysmal dilatations in the proximal portion of the innominate artery.

Case 2. A male aged 20 years who died suddenly, one week after admission to hospital. He was uraemic with a blood pressure of 180/120, and grade 4 retinopathy. The kidneys were small, with granular cortical surfaces. Blocks taken for histology showed a chronic glomerulonephritis. The left ventricular myocardium was normal and "atheroma" was noted in the thoracic aorta. A portion of this was taken for histological examination. The other organs showed no macroscopic abnormality.

Case 3. A male aged 40 years who died suddenly and unexpectedly, and a ruptured aneurysm of the aortic arch was found at post mortem. The specimen submitted showed dilatation of the aortic arch with thickening of its wall, and a grey, wrinkled intima. (Fig. 183).

Cases 4 & 5, were post mortems performed in Rabaul in 1963. Pieces of tissue taken from aortic aneurysms found during these post mortems were submitted for histological examination. No clinical details accompanied the specimens.

Case 6. A male aged 26 years who died from renal failure

due to amyloidosis. He was reputed to have had a previous admission for arthritis but no details of this could be found. At post mortem, the wall of the aorta for the whole of its length was markedly thickened. On the intimal surface there were multiple, round, soft, yellow plaques varying in size from 1 to 5 cms. in diameter, and partially obstructing the lumen of the aorta. The proximal portions of the innominate and left common carotid arteries were thickened and their lumena were severely reduced. The left subclavian artery also had a thickened wall, and the lumen was greatly reduced by the soft, yellowish atheromatous plaque on its intimal surface. (Figs. 184 & 196). The renal arteries were both normal. No evidence of arthritis was seen at post mortem, and histological sections of the synovium from the left knee showed non-specific changes with a light infiltration of mononuclear inflammatory cells. The joint cavity appeared normal macroscopically. No amyloid was found in the aorta or its large branches.

Case 7. A 40 year old woman was admitted to the Port Moresby Hospital for investigation of hypertension and aortic incompetence. She was found to be uraemic, and was thus included in the investigation of uraemic patients admitted to the hospital. (Chapter 3). Her x-rays were reviewed at the author's request. Plain x-rays of the thorax and upper abdomen showed calcification and dilatation of the aorta, and a "coarctation-like" nipping of the aorta just above the diaphragm. (Figs. 185 & 186). The patient was discharged and lost to follow-up.

Case 8. A 15 month old female child died of cardiac failure and a left upper lobe pneumonia. Clinically she was thought to have a patent ductus arteriosus. Only the thoracic contents were submitted

for pathological examination. The aorta down to the diaphragm was markedly thickened as were also the three major aortic arch branches. The pulmonary arteries were similarly thickened. (Figs. 187 & 188). The bronchopneumonia was confirmed. The doctor who performed this autopsy reported that the child's brother had died three days earlier of cardiac failure, and at autopsy an aneurysm of the ascending aorta had been found. Unfortunately it was not preserved for pathological examination.

Case 9. A male aged 53 years who died from acute dysentery. A small aneurysmal bulge in the aortic wall was found just above the diaphragm. Apart from a few small, fatty atheromatous plaques the remainder of the aorta was normal.

Case 10. A male aged 40 years who also died from acute dysentery. At post mortem an aneurysmal bulge in the aortic arch was found. The intimal surface in this area was grey and wrinkled. There was thickening of the walls of the great vessels arising from the arch. (Fig. 189).

Case 11. A male aged 30 years who died from bronchopneumonia, bronchiectasis and acute pericarditis. A small area of aneurysmal bulging was found in the aortic arch. The remainder of the aorta showed no significant abnormality.

Case 12. A male aged 25 years who died suddenly and unexpectedly. A post mortem ordered by the coroner revealed a posterior myocardial infarction, and the thoracic aorta was markedly thickened. No other abnormality was demonstrated.

Case 13. A male aged 30 years admitted with pneumonia. A thoracic aneurysm was noted on chest x-ray. This ruptured a few days after admission and was confirmed at post mortem. The wall of the aorta was thickened and there were many white, wrinkled plaques on the intimal surface. Serum and cerebrospinal fluid were obtained prior to death. A V.D.R.L. and a Treponema immobilisation test were performed on each of these. Both tests were positive in the serum and negative in the cerebrospinal fluid.

Case 14. A 28 year old woman was referred to the Royal Brisbane Hospital for investigation of hypertension (180/100) which persisted after delivery of her third child three months previously. She lived on an island in Torres Strait south of Daru, and she had the physical features of a Papuan. During the performance of an intravenous pyelogram, areas of calcification were noted in the upper abdomen which suggested the presence of calcified aneurysms of the renal arteries. Calcification was also present in the thoracic aorta. An aortogram was performed and this demonstrated multiple aneurysms in the thoracic and abdominal aorta, and in both renal arteries. The superior mesenteric artery was occluded, and a large anastomotic vessel had developed from the inferior mesenteric artery - the so-called "wandering mesenteric artery". (Fig. 190). No symptoms suggesting the presence of intestinal ischaemia were elicited. Serological tests for syphilis (V.D.R.L., Kolmer and Reiter Complement Fixation Tests) were positive. The patient was treated with anti-hypertensive drugs and she was discharged shortly after the aortogram was performed.

Macroscopic Features

These may be summarised as follows:

The earliest lesions consisted in localised areas of aortitis with thickening of the walls, and occlusion of the lumena of the vessels arising from the aorta, particularly the aortic arch. Aneurysms occurred along the length of the aorta and on the large vessels, particularly the renal arteries. The intimal surface of the aorta and its large branches became wrinkled, and the irregular narrowing of the lumena of these vessels resulted from the deposition of atheromatous plaques on the damaged intima. This gave rise to the areas of "coarctation-like" nipping along the length of the aorta, and the partial or complete occlusion of vessels arising from the aorta. Calcification in the wall of the aorta was commonly encountered, and it appeared at an early stage in the evolution of the disease.

Histological Features

In all of the post mortem cases there was thickening of all components of the vessel walls, with gross disruption of the elastic laminae. (Figs. 191, 192 & 195). In all except Case 8 this elastic disruption was accompanied by an ingrowth of small vessels surrounded by mononuclear inflammatory cells. (Figs. 192 & 194). The media in some cases was heavily calcified. There was a moderate degree of inflammatory cell infiltrate around the vasa vasora, and these showed varying degrees of endarteritis obliterans. (Fig. 193). There was marked atheroma of the intima. (Fig. 196). Spirochaetes were searched for in four cases, but none were found. Case 8 showed a similar appearance both in the aorta and in the pulmonary arteries, that is separation

and disruption of the elastic laminae, but without any inflammatory cell infiltration. (Fig. 197). In one of the multiple sections taken from the aorta in Case 6 a small abscess was found in the media. (Fig. 198). No organisms could be demonstrated in this abscess.

Discussion

This series of cases illustrates virtually all the clinico-pathological features that have been described in Takayasu's arteritis, except that there was no preponderance of females as in other reported series. The earliest lesions were seen in coronial autopsies in which death was due to some unrelated condition. More advanced lesions were present in patients dying from the complications of the disease itself. When the author had established that this condition occurred in T.P.N.G. and had demonstrated the clinico-pathological features to be looked for, more cases were diagnosed both at post mortem and during life, as was illustrated by Cases 9-14.

It may be argued that Case 8 does not fit exactly into the group because of the young age, the severe involvement of the pulmonary trunk and the large pulmonary arteries, and the absence of inflammatory cell infiltration in the vessel walls. However, as an example of at least a closely related form of arteritis, it does warrant inclusion here. The fact that this patient's brother died from an apparently similar condition suggested that these two cases of arteritis may have been familial, or perhaps were caused by the same environmental agent. Such an association does not appear to have been reported previously. The absence of histology on one sibling is regrettable, but further cases may occur and should be looked for.

Backhouse (1958) reported 12 cases of atheroma from his series of 724 post mortems performed in Rabual between 1923 and 1934. Histological examination was performed on only two of these cases. Judging from the macroscopic and microscopic descriptions of the aortas, at least seven of these fitted the pattern of Takayasu's arteritis.

Differential Diagnosis

The differential diagnosis of Takayasu's arteritis is from other forms of arterial disease. It can be distinguished easily from atheroma occurring alone because of the disruption of the elastic laminae and the inflammatory cell infiltration. Giant cell arteritis usually involves the temporal arteries. (Harrison, 1948). Giant cells are very seldom seen in Takayasu's arteritis, and were not seen in any case in this series. It can be distinguished from the arteritis occurring in rheumatoid arthritis because none of the patients have had arthritis.

The most difficult differential is from syphilitic arteritis. Turnbull (1914) reviewed 288 cases of syphilis seen at post mortem at the London Hospital between 1908 and 1913. He found 175 cases of syphilitic aortitis. The distribution of these lesions is shown in Table 42.

TABLE 42

Sites of Syphilitic Involvement of Aorta and Its Large Branches in 175 Cases

Aortic commissure	99
Ascending thoracic aorta	160
Arch of aorta	116
Descending thoracic aorta	118
Abdominal aorta	33
Aortic arch vessels	28
Pulmonary arteries	2
Coeliac artery	2
Superior mesenteric artery	2
Splenic artery	1

The histological appearances described are similar to those seen in Takayasu's arteritis. The age and sex distribution of this series of syphilitic arteritis was not given. However, it was recorded that one patient was a girl aged 7 years, and another a girl aged 17 years.

The criteria on which these cases were regarded as being caused by syphilis were:

A history of previous syphilitic lesions, particularly chancres. Such a history was obtained in 34 of the 175 cases.

Wasserman tests which were positive in 35 of the 42 cases tested.

Spirochaetes were searched for in all cases but were present in none.

From this report it would appear that the criteria for diagnosis of syphilitic arteritis were not absolute, and some cases given this label may not have been caused by the Treponema pallidum. The distinction between syphilitic arteritis and Takayasu's arteritis is extremely difficult, if it is possible at all. None of the previously reported cases of the latter have had positive serology for syphilis, and this has been taken as evidence against a Treponemal aetiology. In both cases in which serological tests for syphilis were performed in the present series, they were positive; but among the people of T.P.N.G. this does not necessarily indicate the presence of syphilitic infection. Yaws was widespread throughout the country until a programme was carried out in the early 1950's to inoculate the population with penicillin. However, approximately 40% of the population still have positive Kahn Laughlan tests. (Vines, 1970).

Aetiology

Attempts have been made to ascertain whether yaws can cause arteritic lesions similar to those ascribed to syphilis. (Strong, 1943). These have been inconclusive because no population has been found in which yaws was prevalent but syphilis did not occur. No cases of primary or secondary syphilis were seen in T.P.N.G. in the period under review, but there has been a recent report of an out-break of spirochaetal infection, probably syphilis, in the Highlands. (Rhodes and Anderson, 1970). In view of these observations, the possibility of a syphilitic aetiology cannot be ruled out, and no clear-cut distinction can be made between the effects of yaws and those of syphilis.

Kinare (1970) reported 20 cases of aortitis occurring in Bombay. Tuberculosis was present in 14 of these, and he suggested that the aortitis may have been caused by the tuberculosis. Although tuberculosis was prevalent in T.P.N.G., none of those with aortitis was suffering from this disease. It appears unlikely, therefore, that the aortitis was caused by tuberculosis.

It was suggested by Riehl and Brown (1965) that Takayasu's arteritis might be an autoimmune disease. Serum from case 14 and from a further case examined more recently was tested by the author for the presence of anti-nuclear factor and anti-aorta antibodies using fluorescein labelled anti IgG+IgM. Each of these tests was negative in both cases. This does not altogether rule out the possibility that the aortitis is due to an auto-immune disease, but no auto-antibody was detected by techniques currently being employed in a routine diagnostic laboratory.

Summary

14 cases illustrating the clinico-pathological features described in Takayasu's arteritis have been identified in T.P.N.G. This is the first description of this condition in the Melanesian population of the South Western Pacific.

In the author's view, no distinction can be made between Takayasu's and syphilitic arteritis on morphological grounds. In the cases reviewed from T.P.N.G. a syphilitic aetiology could not be definitely excluded, because serological tests for syphilis were positive in two of them. However, no definite aetiology could be postulated for these cases.

CHAPTER 12

LOCOMOTOR SYSTEM

Infections

Poliomyelitis epidemics occurred sporadically. Almost certainly as a result of this it was a common sight to see among the general population, young adults with paralysis and wasting of large muscles.

Tuberculosis of the spine and the large joints, particularly the knee and the hip, was seen in all coastal areas of the country. During the financial year 1963-64, 104 patients (0.01% of all inpatients) were treated for tuberculosis of bones and joints in the various hospitals in T.P.N.G. (Department of Public Health Hospital Disease Statistics 1963-64 (1967)).

None of these cases came to post mortem examination, but quite a few synovial biopsies were submitted for diagnosis. Material removed during operative treatment of spinal tuberculosis was also submitted for histological examination.

The condition called "tropical myositis" was seen fairly commonly all over the country. This consisted in an abscess forming in almost any muscle in the body, but particularly in the large muscles, and sometimes in more than one muscle. Culture of the pus usually resulted in isolation of Staphylococcus pyogenes. Histological examination revealed muscle necrosis with variable amounts of acute and chronic inflammatory cell infiltration. The clinical manifestations and the surgical treatment have been described. (Clezy, 1966; Radford

and Smith, 1969).

Tumoral Calcinosis

This is a condition characterised by the presence of a calcified mass in the subcutaneous tissue. (Fig. 199 (a)). It is usually mobile, well circumscribed and easily excised. It may occur in more than one site in any individual. Macroscopically it is a well circumscribed tumour, usually spherical. It is gritty to cut, often needing a saw to cut it. The cut surface shows multiple rounded, yellow, calcified nodules each a few millimetres in diameter. These are separated by wide bands of dense fibrous tissue. (Fig. 199 (b)). Histologically there are amorphous masses of calcified material surrounded by dense, poorly cellular fibrous tissue. Usually there is no cellular reaction around the calcified material, but sometimes multinucleated giant cells can be found. (Fig. 200 (a)). In occasional cases bone formation occurs. (Fig. 200 (b)).

This condition has been reported from various parts of Africa where it appears to be relatively common. (McClutchie and Bremner, 1969). Its aetiology has not yet been elucidated. Cases have been recognised in T.P.N.G. (Cooke, 1969) and the illustrations are from personal cases. The details of 16 cases diagnosed during 1966-67 are given below.

There were 10 females and 6 males. The mean age was 32 years, the youngest being 13 years. The anatomical distribution of the lesions was as follows:

Thigh	5
Buttock	5
Hip	4
Elbow	1
Knee	1

All of these were single, but the man with the lesion over the elbow had had similar tumours removed from both buttocks five years previously.

The largest tumour measured 8 x 5 x 4 cms. and the smallest was 1 cm. in diameter. All had been treated by local excision. 11 cases came from the Highlands and the remaining 6 were from coastal areas.

As always, histories were difficult to obtain, and at the time of histological reporting, each referring doctor was questioned, but no specific aetiological factor could be identified. There did not appear to be any particular correlation between previous injections at the site, or previous trauma.

The importance of these cases was the realisation that the condition occurred fairly frequently in the people of T.P.N.G. as well as in those of Africa. Further study of individual cases may reveal information about the pathogenesis of this curious condition.

Muscular Dystrophy

The author examined a number of muscle biopsies from patients with pseudo-hypertrophic muscular dystrophy. Studies are currently

being carried out in Port Moresby on a small number of families with this condition. Females as well as males are affected. The muscle weakness appears at 2 or 3 years of age. Some muscles, e.g. calf muscles are obviously enlarged, and creatine phosphokinase levels are grossly elevated. (Biddulph and Gooch, 1969).

Arthritis

Maddocks (1967) reported a number of cases of Reiter's syndrome from Port Moresby. Jeremy et al (1969), reported from Goroka 22 cases of a monoarticular arthritis which was unassociated with manifestations of severe systemic illness, and which did not fit into any group of arthritides previously recognised. The arthritis associated with Reiter's syndrome was the most common form of arthritis seen in Port Moresby. The arthritis syndrome described by Jeremy et al. was the only form of arthritis commonly seen in Goroka. No cause for these forms of arthritis has been determined, and no reason for their unusual prevalence in T.P.N.G. has been ascertained.

Cases of gouty arthritis, osteo and rheumatoid arthritis were recognised, but occurred much less frequently than the forms of arthritis mentioned above. The author examined synovial biopsies from about 30 cases of various forms of arthritis, and apart from those with gout, tuberculosis and a few with classical rheumatoid disease, no specific features were noted.

Tumours

Bone Tumours

Virtually the whole range of possible tumours, benign and malignant, were seen. Malignant bone tumours, the commonest of which was osteogenic sarcoma, accounted for 2.0% of all tumours in both males and females. This figure does not include primary jaw tumours which were recorded separately.

Soft Tissue Tumours

Benign soft tissue tumours were frequently observed, but their prevalence was not specially recorded. Those presenting for treatment were always large. The patient illustrated in Fig. 201 was suffering from a juvenile nasopharyngeal angiofibroma, a benign soft tissue tumour which was encountered about once a year.

Keloid scars were frequently seen. Sometimes they resulted from accidental trauma such as burns (Figs. 202 & 203), and sometimes they were specially produced for their decorative effect. Judging from the frequency with which they appeared in the surgical pathological material, keloid scars on the ear lobes were common. Presumably they resulted from ritual perforations, and were not regarded as being particularly decorative. (Fig. 204).

Malignant soft tissue tumours accounted for 2.5% of all tumours notified. A wide variety of tumour types was observed. Many of these were virtually impossible to classify. No particular pattern of prevalence was noted. The tumour illustrated in Fig. 205 was a

circumscribed mass in the forearm of a four year old boy. This shelled out easily at operation. Histological examination revealed an alveolar rhabdomyosarcoma. Fig. 206 shows the tumour three months after removal of the primary. No pulmonary secondaries were noted at this time and the arm was amputated. He returned to his home, and as so often happened, he was lost to follow-up.

CHAPTER 13

CENTRAL NERVOUS SYSTEM AND EYE

Central Nervous System

Infections

Meningitis was an important disease in T.P.N.G. From 1960 to 1964 it ranked fourth among the principal causes of death, accounting for between 5.3 and 5.8% of deaths in those years. During 1963-64 0.6% of the 114, 152 in-patients treated in the various hospitals were suffering from meningitis. (Department of Public Health Hospital Disease Statistics 1963-64 (1967)).

Among the 1,100 post mortems examined in the Pathology Department, Port Moresby from 1962-67 there were 25 cases of meningitis. These included children and adults. These cases were divisible into three groups:

Pyogenic meningitis (no specific organism recognised)	15
Tuberculous meningitis	6
Torula (Cryptococcal) meningitis	4
	25

Eight of the cases of pyogenic meningitis were children under the age of 10 years, while the other 7 were adults over the age of 20 years. In 5 cases pneumonia was present as well as the meningitis. The ages of the 6 cases of tuberculous meningitis were: 8 months, 12, 16, 22, 24 and 47 years. In only 3 cases was the meningitis not part

of a disseminated infection.

The ages of those with torula meningitis were: 1 month, 28, 30 and 40 years. In no case was there any evidence of immune-paresis or any predisposing debilitating disease. In none of these cases was any organ other than the brain involved.

Only one review of the bacteriology of meningitis in T.P.N.G. has so far been published. (Biddulph et al, 1968). This was a review of the features of 108 cases of meningitis admitted to the children's ward of the Port Moresby General Hospital during a three year period between 1964 and 1967. The bacteriology quoted was done by the technical staff in the author's laboratory. An organism was isolated in 68 cases. The frequency with which each organism occurred is shown in Table 43.

TABLE 43

Bacteriology of 68 Positive CSF Cultures in Children

Organism	% of the Positive Cultures
Neisseria meningitidis	53
Diplococcus pneumoniae	20
Haemophilus influenzae	19
Staphylococcus pyogenes	3
Streptococcus pyogenes	3
Proteus	2

Cases of tuberculous meningitis were excluded from the above series.

The three commonest organisms isolated from the CSF's of children with meningitis were also the most common organisms isolated from adult cases. Unfortunately the author has no data as to the relative frequency of isolation of these different organisms from the adult cases. Tuberculous meningitis and torula meningitis occurred so regularly that it was a routine practice in the laboratory to do a Ziel Neilsen stain and an Indian Ink preparation on any C.S.F. which contained mononuclear cells, and to culture these for TB and torula as well.

A survey of the bacteriological results obtained from 454 positive cultures of C.S.F. specimens from patients in the Royal Brisbane Children's Hospital between 1958 and 1968 was recently performed. (Forgan-Smith, 1969). The results are shown in Table 44.

TABLE 44

Bacteriology of 454 positive C.S.F. Cultures
Royal Brisbane Children's Hospital

Organism	% of the Positive Cultures
Haemophilus influenzae	38.0
Diplococcus pneumoniae	9.0
Neisseria meningitidis	10.5
Staphylococcus pyogenes	4.5
Staphylococcus albus	14.0
Enterobacteria	11.2
Other gram negative organisms	7.0
Streptococcus	4.0
Miscellaneous	1.8

Haemophilus influenzae was the commonest organism isolated in Brisbane, while Neisseria meningitidis was the most common one in Port Moresby. The staphylococci in the Brisbane series was isolated mainly from children being treated surgically for hydrocephalus.

Other infections of the central nervous system were seen much less commonly, e.g. cerebral abscess, encephalitis and cerebral malaria. An important, though fairly rare condition, was tuberculoma. (Fig. 210).

Vascular Conditions

Haemorrhage

Cases of cerebral haemorrhage seen in the post mortem series were as follows:

Subarachnoid haemorrhage from ruptured cerebral aneurysm	3
Intracerebral haemorrhage ? from hypertension	2
Haemorrhage from a haemangioma of the cerebellum	1
Haemorrhage from invasion of the base of the brain by a juvenile naso-pharyngeal angiofibroma	1

A few cases of spinal subarachnoid haemorrhage from spear wounds were encountered.

Infarction

Two of the Port Moresby post mortems were on patients who died from acute cerebral infarction as a result of cerebral artery thrombosis. Both were males, one aged 45 and the other 50 years. This complication of atherosclerosis was distinctly uncommon. (see Chapter 11).

Tumours

Only a few neoplasms were seen. These included gliomas and chromophobe adenomas of the pituitary. A few spinal cord tumours - neurofibromas and meningiomas - appeared in the surgical pathology material.

An important differential diagnosis of cerebral tumour was cerebral tuberculoma. The author was aware of a few cases which were diagnosed on clinical grounds - signs of an intracranial space occupying lesion with fever, and sometimes evidence of tuberculosis elsewhere. The files of the Pathology Department of the Royal Brisbane Hospital contain sections from three cases referred to Brisbane for neurosurgical treatment of a "cerebral tumour". The author found one tuberculoma in a post mortem on a thirteen year old girl who was diagnosed clinically as having a cerebral neoplasm. (Fig. 210).

Skull Abnormalities

Two unusual skull deformities were noted in post mortems performed personally. In both cases death was due to some completely unrelated pathology. Both were females. In one there was a deep indentation across the vault of the skull running in an antero-posterior direction. It appeared to be a healed fracture, possibly resulting from an axe wound. The other consisted of a round hole through which the scalp and the dura were adherent to each other. There was a tongue of thin membrane bone growing across from one edge of the hole. This appeared to be a healing trephine hole. No history about this could be obtained, and it is remotely possible that it could have been done in a hospital. However, this observation may have had some

anthropological significance if it could have been shown that it had been done as some form of ritual. Scratching the forehead (Fig. 53) for example, was a well known remedy for head pain in some parts of T.P.N.G., and perhaps trephining the skull may have had a similar rationale.

Kuru

This is a familial cerebellar ataxia occurring with high frequency amongst the Fore and adjacent language groups in the eastern Highlands of T.P.N.G. It is fatal within two years of the onset of symptoms. It affects mainly adult women and younger people of both sexes. A kuru-like syndrome has been induced in chimpanzees by intra-cerebral inoculation with extracts of brain from fatal cases of kuru. This has been interpreted as indicating that it may be caused by a "slow-virus". From anthropological evidence it is thought that the disease may have been transmitted through the practice of Fore women eating the brains of other deceased female members of the clan. (Zigas and Gajdusek, 1957; Gajdusek et al, 1966; Mathews, 1968). The author had no personal experience with this disease.

Comment

Neuropathology was under-represented in the period of this survey because none of the surgeons was particularly interested or skilled in this field, and there was no practising neurologist in T.P.N.G. All cases requiring neurosurgical treatment were sent to Brisbane, and no record of the pathology from such cases was received in Port Moresby. As these deficiencies are remedied, and as x-ray

equipment becomes available for the performance of cerebral angiography and air encephalography, more neuropathological conditions will be diagnosed.

Eye

Trauma

Penetrating injuries to the eye were fairly common as a result of the living conditions and way of life of the people. Phthysis bulbi was the commonest pathological lesion for which eyes were removed and submitted for histological examination. These eyes showed varying degrees of disorganization.

Tumours

Eye tumours, almost all of which were retinoblastomas (Fig. 207), accounted for 1.2% of all the tumours notified. This percentage supported the clinical impression that retinoblastomas were more frequent in T.P.N.G. than in countries like Australia. Frequently the tumour had extended beyond the confines of the globe at the time of enucleation. (Fig. 208). Apart from their apparent frequency and the advanced stage of the disease at the time of presentation, there seemed to be nothing unusual about them. Their behaviour and histology seemed to conform to the well recognised patterns.

Some Burkitt lymphomas presented as eye tumours as was mentioned in Chapter 5.

A few squamous carcinomas of the cornea were submitted for histological examination. One occurred in a ten year old girl with

xeroderma pigmentosa. (Fig. 209 (a)). Other cases were seen in adults. Histologically these were well differentiated and did not appear to be producing deep penetration, but rather an exophytic growth. (Fig. 209 (b)).

About half a dozen "mixed" tumours (pleomorphic adenomas) of the lacrymal gland were examined. Some of these were in children.

CHAPTER 14

FEMALE GENITAL SYSTEM

Infections

Vulvo-vaginal donovanosis and amoebiasis were relatively common and are dealt with in Chapter 9. Trichomonas vaginitis was quite common, but demonstrated no special features. Wilkey and Johnson (1971) reported four cases of vulval herpes simplex infections.

Chronic salpingitis and pelvic abscess were very common in all parts of the country and many operative specimens of chronic salpingitis were submitted for histological examination. These were most commonly associated with post partum infection. Tuberculous salpingitis and endometritis were occasionally encountered.

Abnormalities of Pregnancy

Retained Placenta

Retained placenta was one of the most common obstetrical problems confronting doctors in all parts of T.P.N.G. Women would be brought to hospital some days after confinement because the placenta had not yet been passed. The village midwives had devised various ways of dealing with this. The method illustrated in Fig. 211 (a) involved tying a coconut to the end of the umbilical cord to provide constant traction. (Cave, 1970).

Medical practitioners with experience of this problem agreed that conservative management was the safest and most effective way of

dealing with it. If the patient was given antibiotics and blood transfusion (if this was indicated) the placental remnants would eventually be absorbed or passed in fragments. Attempted manual removal of the placenta under such circumstances frequently led to uncontrollable haemorrhage. Quite a few uteruses removed at hysterectomy when manual removal had been unsuccessful were submitted for histological examination with a clinical diagnosis of placenta accreta. An occasional one of these was a true placenta accreta, but most of them appeared to be simple retained placentas. Severe post partum haemorrhage resulting from fibrinolytic overactivity appeared to be unusually common, (Booth and MacGregor, 1967) and this was a further hazard in the treatment of retained placenta.

Clostridium welchii infection was occasionally encountered as a complication of retained placenta. The placenta illustrated in Fig. 211 (b) was from a personal autopsy performed on a young woman who was admitted to hospital in a moribund state. She had delivered one week prior to admission. Her haemoglobin was barely recordable and the peripheral blood film showed a haemolytic anaemia. She had gas gangrene of the uterus together with acute peritonitis.

Extra-uterine Pregnancy

Intra-abdominal pregnancy was occasionally encountered. (Kariks, 1960; Powell and Rich, 1969; Smith, 1969). Fig. 212 shows a very advanced tubal ectopic pregnancy which was submitted for examination. The usual variety of ectopic pregnancy was encountered quite frequently, but no estimate could be made as to its prevalence in this population as compared with any other population group.

Abnormalities of Twin Pregnancy

Conjoined Twins

Two pairs of conjoined twins were submitted to the author for examination. One pair consisted of two fairly symmetrical bodies joined anteriorly from the manubrium sterni to just above the pubis. (Thoracopagus). The second consisted of a double headed monster. (Dicephalus dipus dibrachius). Both specimens were preserved for museum mounting and were not dissected in detail.

Foetus-in-foetu

This is the rarest abnormality of twin pregnancy and occurs when one of a pair of conjoined twins is actually incorporated within the body of the other. Willis (1960) distinguished this condition from a teratoma by the fact that the parasitic foetus possessed a spine and a plainly somatic distribution of parts, whereas in a teratoma the various tissues are not arranged in any orderly fashion.

The author had four probable cases of this condition referred by surgeons for pathological examination.

Case Histories

Case 1. An excellent example of this condition was submitted for examination in 1968 (Smith, 1969). The parasitic foetus was removed from a gestation sac in the retroperitoneal region of the upper abdomen of a two year old female child. The diagnosis was made pre-operatively when foetal parts were demonstrated on plain x-ray of the upper abdomen. The parasitic foetus had a large cystic cavity at its cranial end. This

was lined by choroid. A "face" and teeth were present on the ventral surface of this cyst. There were four rudimentary limbs and a vertebral column. Internally there was a single coelomic cavity lined by colonic type epithelium. (Figs. 213 and 214).

Case 2. A second, rather similar case was recognised a few months after the first one. It presented as an upper abdominal mass in a one year old male child. It was removed, together with the gestation sac, from its retroperitoneal position in the host. It had a less foetoid appearance than the first case, but was covered by skin which also contained skin appendages.

A cranial and a caudal end could be recognised. On one outer surface at the cranial end there was an oval, black area 2 x 1.5 cms. This resembled choroid of the eye. At the caudal end there was a small pit in the skin, surrounded by tufts of long hair. It resembled a sacral pit. X-ray revealed at the cranial end a calcified mass which contained structures resembling teeth. (Fig. 215). Poorly developed vertebrae were identified in a section through its long axis. (Fig. 216). Between this and the umbilical leash there were a number of loops of "intestine" lined by colonic type epithelium. The main bulk of the "foetus" consisted of adipose tissue.

Attached to the outer surface of the gestation sac and separate from the "foetus" there was a second tumour mass, one portion of which had a smooth surface. (Fig. 217). On sectioning, this proved to be a layer of stratified squamous epithelium which in places was cornified. Beneath this portion there was a hard mass which on x-ray consisted of a calcified area together with a well formed tooth. (Fig. 217 (b)). A slice through an adjacent area of the mass showed a mass

of yellow, homogeneous material and a few cysts filled with clear mucoid material. (Fig. 217 (a)). The large cyst was lined by stratified squamous cornified epithelium and respiratory epithelium. Sections from the homogeneous material showed a wide range of tissues including brain, choroid plexus, cartilage, bone and haemopoietic marrow.

This was interpreted as being a foetus-in-foetu enclosed in a gestation sac to which was attached a teratoma.

Case 3. In Port Moresby in 1962 a male child aged 18 months presented with a large abdominal tumour. Plain x-ray of the abdomen showed what appeared to be a number of small bones. At operation a well encapsulated tumour was found attached by a small pedicle to the posterior abdominal wall at the upper pole of the right kidney. It received its blood supply from the right renal artery. The whole tumour was easily removed. It consisted of a spherical mass 13 cms. in diameter enclosed within a sac. When the sac was removed, half the circumference of the tumour was covered by what appeared to be skin covered by vernix caseosa. At the pedicle end of the tumour there was a sausage shaped, soft, twisted structure which microscopically was lined by alimentary tract epithelium. Also at this end of the tumour five small digits were recognised. These were attached to what appeared to be a wrist, and transverse section at this point revealed two bones, one of which was flat and resembled a radius, and the other was round, resembling an ulna. The digits were markedly deviated to one side so that they were running almost at right angles to the direction of the "arm" bones.

X-ray of the tumour (Fig. 218) confirmed the presence of five phalanges, what appeared to be wrist bones, and a possible radius and ulna. Other unidentifiable bones were also present. Section through the tumour revealed that the portion containing the bones consisted of firm, rather homogeneous, yellow tissue. The other half contained multiple cysts filled with mucoid material. Sections taken from various parts of the tumour revealed alimentary tract, brain, respiratory mucosa, smooth muscle, nerves and bone.

Case 4. In 1966 a two months old male child was born with what appeared to be an exomphalos. When the sac was opened, it was found to contain a well formed lower limb and portion of a pelvis. (Fig. 220). X-ray revealed a pelvic bone, femur, tibia and fibula, tarsal and metatarsal bones and phalanges. A loop of "intestine" was present in the "pelvis", and the skin covering this area superficially resembled external genitalia. The sac extended into the child's upper abdomen and was left in situ after the leg was removed.

Discussion

Foetus-in-foetu is an extremely rare condition. Grant and Pearn (1969) reported a case in a child of a Tongan couple. They found only 15 previously reported cases, and they estimated that the abnormality occurred with no greater frequency than once in 500,000 births.

The finding of four cases in such a relatively short space of time suggests either that the abnormality is more prevalent in the population of T.P.N.G. than elsewhere, or that the diagnostic criteria used in these cases were not sufficiently stringent. If the cases are

not regarded as being true foetuses-in-foetu, they would have to be called retroperitoneal teratomas showing a remarkable degree of organ differentiation. Even this condition would be extremely rare. (Willis, 1960).

In the author's opinion all four cases could be regarded as foetuses-in-foetu because of their extremely advanced organ differentiation and somatic distribution of parts.

Case 2 consisted of two masses of tissue, and could be regarded as a teratoma attached to a foetus-in-foetu. Such an association has not been described previously.

Hypoxia has been implicated as a cause of congenital anomalies (Ingalls, 1960). It has been shown that the prevalence of patent ductus arteriosus increases with altitude in the Andes Mountains in Peru. (Alzamora et al, 1953). Two of the foetuses-in-foetu occurred in the Highlands. One was from the south coast and the other from the north coast. That all four were due to the teratogenic effect of hypoxia can therefore be discounted.

The different tribal groups in T.P.N.G. have been relatively isolated from each other for centuries, and a high prevalence of genetically determined disorders has been noted, e.g. haemoglobinopathy (Ryan, 1961 and Booth, 1966) and albinism (Walsh, 1967). Perhaps the prevalence of foetus-in-foetu could be related to the degree of inbreeding. But if this were so, more case reports from other countries would have been expected than can be found in the literature.

Some environmental teratogenic agent may have been operating, but no information regarding this possibility was obtained in these

four cases.

Summary

Four probable cases of foetus-in-foetu were examined personally. No satisfactory explanation for this apparently high prevalence was obtained.

Tumours

Uterus

Carcinoma of the cervix accounted for 70% of cancers of the female genital tract. Skin cancer was the most common form of cancer in women, but carcinoma of the cervix was second, accounting for 13.8% of all cancers in women. Standards of hygiene were low; sexual intercourse began at an early age; and among some communities promiscuous intercourse was common. It was not surprising, therefore, that cervical cancer was relatively common. At the time of presenting for treatment the disease was always far advanced. (Fig. 221).

Adenocarcinomas of the body of the uterus were very rare, only one or two cases being encountered by the author.

A few cases of carcinoma of the vulva were seen. These were usually squamous carcinomas, but two adenocarcinomas appeared in the surgical pathological material.

One embryonal rhabdomyosarcoma of the cervix was diagnosed in a child four months of age by histological examination of blood clot passed into a napkin. Total hysterectomy was performed and the child

was alive and well two years later.

No special record was made of hydatidiform moles. About 20 were seen each year in the surgical pathology specimens. Approximately four or five chorionepitheliomas were seen each year. This was a greater prevalence than was encountered in Brisbane, Australia (personal observation), but was a lesser prevalence than that encountered among Chinese communities. (Joint Project for the Study of Choriocarcinoma and Hydatidiform Mole in Asia, 1959).

Of the benign tumours of the uterus, fibroids and adenomyosis were seen occasionally. Fibroids were commonly encountered in African women, (Davies, 1959) but they were relatively rare in T.P.N.G.

Ovary

Benign mucinous cystadenomas and simple serous cystadenomas were commonly seen and they often attained huge dimensions. (Fig. 222). A moderate number of dermoid cysts were also encountered.

Malignant ovarian tumours accounted for 7.3% of all tumours in women. 65 cases were collected between 1958 and 1967 and the majority of these were personally reviewed. The types seen are listed in Table 45.

TABLE 45

Ovarian Cancers 1958 - 67

Papillary cystadenocarcinoma	23
Dysgerminoma	12
Mucinous cystadenocarcinoma	12
Solid adenocarcinoma	5
Krukenberg tumours	3
Arrhenoblastoma	2
Brenner tumour	1
Burkitt's lymphoma	1
Undifferentiated carcinoma	4
Unclassifiable	2
	65

These tumours came from all geographical regions of T.P.N.G. with no special prevalence in any particular region.

One of the most interesting features was the prevalence of dysgerminoma. This relatively high prevalence was also noted in Africa (Davies, 1959). The ages of the present cases ranged from 10 to 30 years. Most of the tumours were very large when first diagnosed, and metastatic spread had already occurred.

Breast

Infections

Inflammatory conditions included breast abscesses. Sometimes these were difficult to distinguish from carcinomas both on clinical and histological evidence. In such cases the breast was enlarged and hard, sometimes with ulceration through the skin. Biopsy revealed masses of histiocytes which could be confused with cells of a colloid carcinoma. (Fig. 223).

The young woman illustrated in Fig. 224 had miliary tuberculosis. Antituberculous therapy failed to reduce its size. A simple mastectomy was performed, and histological examination revealed the presence of tuberculous mastitis.

Tumours

Breast cancer accounted for 10.7% of all cancers in women. They were usually Stage 3 or 4 at the time of diagnosis. (Figs. 225 & 226). It was impossible to determine the exact prevalence of this disease in the community and thus to make comparisons with other countries. It has been suggested that breast cancer is more prevalent among nulliparous women and among those who have never suckled their children than among those who have done so. (Willis, 1960). The women of T.P.N.G. usually began child bearing in their late teenage, and breast feeding was invariable except for a very small number of women living under urban conditions.

Benign tumours included fibroadenomata. Two adenomata of

sub-areolar ducts were encountered, one in a girl aged 14 years and the other in a 26 year old woman.

Sociology

An observation of sociological importance was that in the Highlands, women were sometimes observed suckling piglets. (Fig. 227). (Cave, 1970). This reflected the importance of pigs in the cultural life of the people.

Summary

Infections, vulvo-vaginal and pelvic were common causes of gynaecological pathology. Abnormalities of pregnancy were commonly encountered by medical practitioners throughout T.P.N.G. Those which came to the notice of the pathologist included complications of retained placenta, ectopic pregnancies and abnormalities of twin pregnancy. Four cases of probable foetus-in-foetu were encountered.

Carcinoma of the cervix was the commonest malignant neoplasm of the female genital tract. Carcinoma of the body of the uterus was very rare. Hydatidiform moles and chorionepitheliomas appeared to be more prevalent than in Australia but were much less prevalent than in some parts of Asia. Dysgerminoma was one of the commoner malignant ovarian tumours encountered.

Breast cancers and breast abscesses were relatively common, and were the commonest examples of breast pathology.

CHAPTER 15

RESPIRATORY SYSTEM

The two most commonly encountered diseases of the respiratory tract were pneumonia and chronic lung disease causing cor pulmonale. From 1960 to 1964 pneumonia and malaria were the commonest reason for admission to hospitals throughout T.P.N.G. They each accounted for approximately 10% of all admissions during those years. Pneumonia was by far the most common cause of death throughout this period, accounting for about 20% of all deaths. It was also the most common cause of death in children under 10 years of age, accounting for between 24 and 29% of all deaths in children during that period. (Department of Public Health Hospital Disease Statistics, 1963-64 (1967)).

The importance of pneumonia as a reason for admission to hospital was emphasised by Campbell and Arthur (1964) who found that pneumonia was the commonest cause of admission to the adult medical ward of the Port Moresby General Hospital. 17% of the 2,000 admissions were for pneumonia. Douglas and Riley (1970) reported the clinical, radiological and bacteriological features of 99 patients admitted to the adult ward of the Lae Base Hospital. An account of the clinical features of acute infection of the lower part of the respiratory tract in children was reported by Lawson (1967). These clinical studies demonstrated that pneumonia as encountered in T.P.N.G. resembled that seen in western countries in the pre-antibiotic era, rather than that encountered by physicians in such countries at present.

The report by Douglas and Riley (1970) was the most detailed clinical investigation. They demonstrated that the vast majority of

cases were of the lobar type of pneumonia, and that a little more than half the cases had more than one lobe involved at the time of admission. They confirmed the observation of Campbell and Arthur (1964) that jaundice was a common complication, occurring in 12% of their patients, and, as was the case in Port Moresby, toxic hepatitis from lobar pneumonia was the commonest cause of jaundice admitted to their hospital. Pneumococci were demonstrated in the cultures of sputum from 89% of the adult cases of pneumonia. Of 69 positive sputum cultures in the children, 14 were pneumococcus, 15 haemophilus influenzae, 11 were Staphylococcus aureus and the remaining 29 consisted of a variety of organisms, mostly gram negative bacilli. Both clinical studies demonstrated the effectiveness of penicillin in the treatment of pneumonia, and the treatment of such cases in hospital was accompanied by a very low mortality.

As mentioned in Chapter 11, cor pulmonale resulting from chronic respiratory disease was a common and important form of cardiac disease; but prior to 1965 there had been no investigation of the pulmonary aspects of this. A clinical study of 63 patients with chronic non-tuberculous lung disease who were attending an out-patient clinic in Port Moresby was reported by Alpers (1968). He concluded that the clinical and physiological characteristics of patients with chronic bronchitis and emphysema did not appear to differ qualitatively from similar series in other centres of the world. He was unable to determine the prevalence of this condition in the community because his patients were selected by the fact that they were attending an out-patient clinic. Woolcock and Blackburn (1967) in a preliminary epidemiological survey of people living in the eastern and western

Highlands found that chronic lung disease was relatively common after the age of 30 years. Vines (1970) found clinically recognisable chronic bronchitis and/or emphysema in 5.4% of people over the age of 45 years in the Highlands region, 16.4% in the coastal regions and 17.5% in the Islands region.

No study of the pathology of pneumonia or chronic non-tuberculous lung disease has so far been reported. The following is a record of the author's observations on these two subjects.

Pneumonia

Material

The summaries of the 1,100 post mortems in the file of the Pathology Department in Port Moresby from 1962 to 1967 were reviewed and 171 cases of non-tuberculous pneumonia were found. Approximately 60 of these were post mortems performed by the author. The rest were blocks of tissue referred from all over T.P.N.G. for histological examination. Expatriates and neonates were excluded from this study. Information regarding the pulmonary lobes involved by the pneumonia, and associated features such as jaundice, meningitis, pericarditis and lung abscess were absent from the cases referred for histology from other centres.

Results

Very few of the author's own cases had been admitted to the hospital before death. The majority were coronial autopsies performed on people who died unexpectedly. None of these therefore had had any

specific treatment before death. The vast majority of the cases in both children and adults were lobar rather than broncho in distribution.

Of the 171 cases of pneumonia 121 were males and 50 were females. 46 cases were children under the age of 10 years.

Bacteriological examination was performed on only a very small number of cases. Most of them had no histological features to suggest that they were caused by any specific organisms. However, one young man who was found dead in his house in a village close to Port Moresby had pneumonia and acute cholecystitis. Pure cultures of pyocyaneus were grown from the gall bladder and from the lungs. Another male aged 26 had a pneumonia as part of a generalised chicken-pox infection, and at least one child had a "giant cell" type of pneumonia. suggesting a viral aetiology.

Some features noted among the 60 post mortems performed personally were as follows:

Acute Red Hepatization

This striking macroscopic and microscopic manifestation of pneumonia was observed in two young adult males, each of whom was in his mid-twenties. They both succumbed within 24 hours of becoming ill.

Complications

Complication	No. of Cases	Complication	No. of Cases
Pericarditis	6	Jaundice	4
Lung Abscess	6	Empyema	4
Meningitis	5		

Discussion

Unfortunately the records available for study of this subject were incomplete. Nevertheless a number of observations can be made:

Non-tuberculous pneumonia accounted for approximately 16% of the autopsies. This accords well with the statistics obtained by examination of death certificates, which indicated that pneumonia accounted for 20% of all deaths throughout the country. (Department of Public Health Hospital Disease Statistics, 1963-64 (1967)).

Because so few of these cases had received any treatment they were presumably at a more advanced stage of the disease than were the cases recorded in the two clinical investigations of pneumonia. Complications such as pericarditis, lung abscess, meningitis and empyema occurred in approximately one third of the post mortem cases. Jaundice from toxic hepatitis was present in approximately 6% of them. Although no detailed bacteriological examinations were performed there was no evidence to conflict with the results of bacteriological investigations of sputum reported by Douglas and Riley (1970) and Lawson (1967). They found that the pneumococcus was the commonest infecting organism, with a variety of other organisms being less important.

This post mortem study emphasises the observations made by Douglas and Riley that the manifestations of pneumonia in T.P.N.G. are similar to those which were well known to doctors practising in the pre-antibiotic era.

Summary

Some of the features noted in 171 cases of pneumonia seen at autopsy are reported. Lobar pneumonia was the commonest type encountered. Jaundice from toxic hepatitis was observed in approximately 6% of the post mortems performed by the author, and pericarditis, lung abscess,meningitis and empyema were present in about one third of them.

Chronic Non-Tuberculous Pulmonary Disease

Material and Methods

Between January 1966 and January 1967 an attempt was made to preserve one lung from each post mortem performed in Port Moresby on people over 15 years of age. During this period lungs were preserved from 34 of a possible total of 79 post mortems. From February to December 1967 lungs were collected only from people over 50 years of age. Three lungs were preserved from a possible four such post mortems. A further five lungs were preserved from post mortems performed in Goroka, which meant that 42 lungs were available for study. The main reasons why some lungs were not preserved were: lack of time because of pressure of work, the presence of pulmonary tuberculosis, laceration of the lungs during removal, or damage from trauma such as traffic accidents, and severe disease, such as bilateral pneumonia.

When a lung was removed the main bronchus was left long. The lung was then inflated with 10% formalin from a container situated approximately 30 cms. above the lung. After inflation the main bronchus was tied and the lung was left floating in formalin. During

December 1966 and December 1967 the pressure fixed lungs were sliced in slices 8 mms. thick using a board on which 2 rails 8 mms. in height were fixed. They were then impregnated with barium sulphate and the percentage of emphysema present was estimated by the "point-sampling method" described by Anderson and Dunnill (1965). A grid similar to their grid B with points placed 1.3 cms. apart was used for this estimation. Representative slices of each lung were photographed under water and prints approximating the original size of the lung slices were made to provide a permanent record. This method of preparation of the lung slices was based on that described by Heard (1958). The terminology used in describing the types of emphysema was that used by Heard and Izukawa (1964).

The author was assisted in the examination of these lungs by a vacation-employed student, I. Toogood. The large prints were prepared in the Department of Medicine, University of Sydney with the assistance of Professor C.R.B. Blackburn.

Results

The average percentage of emphysema by age and sex in the 42 lungs examined is shown in Table 46. This demonstrated an increase in the amount of emphysema with increasing age, particularly after age 30 years.

TABLE 46

Average % of Emphysema by Age and Sex

Age (Years)	Total No. Cases	Males		Females	
		Av. % of Emphysema	No. of Cases	Av. % of Emphysema	No. of Cases
< 19	2	0	2	-	0
20-29	19	0.1	19	-	0
30-39	4	1.8	2	0.5	2
40-49	4	0.8	4	-	0
> 50	13	13.6	10	9.8	3
	42		37		5

The cases were then divided according to whether the patients had been born and lived most of their lives in the lowland area around Port Moresby, or in the Highlands. The average percentage of emphysema present in these two groups of cases by age and sex are shown in Tables 47 and 48.

TABLE 47

Average % of Emphysema Lowland Cases

Age (Years)	Total No. Cases	Males		Females	
		Av. % of Emphysema	No. of Cases	Av. % of Emphysema	No. of Cases
< 19	2	0	2	-	0
20-29	14	0.1	14	-	0
30-39	3	3.7	1	0.5	2
40-49	2	0.6	2	-	0
> 50	11	13.6	9	13.0	2
	32		28		4

TABLE 48

Average % of Emphysema Highland Cases

Age (Years)	Total No. Cases	Males		Females	
		Av. % of Emphysema	No. of Cases	Av. % of Emphysema	No. of Cases
< 19	0	-	0	-	0
20-29	5	0	5	-	0
30-39	1	0	1	-	0
40-49	2	1.0	2	-	0
> 50	2	0.2	1	3.3	1
	10		9		1

The increasing prevalence of emphysema with age is well demonstrated in the lowland cases. The Highland group was too small for any firm conclusions to be drawn, but it would seem that the prevalence of emphysema may be less in this group than in the lowland one.

The eleven lowland cases whose age was 50 years or more at the time of death were selected for comparison with a group of 50 cases studied in London, United Kingdom by Heard and Izukawa (1964). The average age of the latter cases at the time of death was 61 years. The details of the cases from T.P.N.G. are given in Table 49.

TABLE 49

Details of 11 Lowland Cases 50 Years of Age or Over

Case No.	Sex	Age (Yrs.)	Height (Inches)	Heart Weight (Grams)	R. ventricle measured at the conus (mm.)	Lung Weight (Grams)	Lung Examined	% of Emphysema	Type of Emphysema	Other Data
1	M	60	63	310	2	R 370 L 480	Right	21.8	Pan acinar destructive	Death from traffic accident. No other significant pathology found.
2	M	60	64	220	3	R 600 L 550	Left	30.0	Pan acinar destructive with bullae up to 4.5cms. diameter at the apex (Fig. 228)	Coronial autopsy. Patient dead on arrival at hospital. A right lobar pneumonia complicated the emphysema.
3	M	64	62	250	3	R 250 L 220	Left	22.0	Centrilobular destructive	He had at least one previous hospital admission for chronic bronchitis and bronchopneumonia. A peak flow recording on that admission was 100. The right lung showed emphysema with patchy areas of bronchopneumonia.
4	M	58	56	250	4	R 520 L 410	Right	53.1	Pan acinar destructive (Fig. 229)	Productive cough, sputum and dyspnoea for a few mths. together with cor pulmonale. At post mortem there was gross mucus plugging of the bronchi.

TABLE 49 (continued)

Case No.	Sex	Age (Yrs.)	Height (Inches)	Heart Weight (Grams)	R. ventricle measured at the conus (mm.)	Lung Weight (Grams)	Lung Examined	% of Emphysema	Type of Emphysema	Other Data
5	M	60	64	Not weighed	5	R 650 L -	Left	7.1	Pan acinar destructive	Had chronic bronchitis and exertional dyspnoea for some years. Lobar pneumonia present in the right lung.
6	M	65	63	250	2	R 650 L 620	Right	2.0	Small irregular patches	Admitted with abdominal pain and fever the day before death. Post mortem revealed an acute bacterial endocarditis involving the tricuspid valve. There was bronchopneumonia in the left lung together with two localised pulmonary infarcts in the lingular segments. There was a pulmonary infarct in the apical segment of the right lower lobe.
7	M	60	60	220	2	R 350 L 260	Left	None found	-	Killed by stabbing with a pick axe.
8	M	55	60	-	-	R - L 600	Right	None found	-	Coronial autopsy because dead on arrival at hospital. The left lung showed lobar pneumonia particularly in the upper lobe which contained an abscess approximately 6 cms. diameter. There was early consolidation of the lingular and lower lobes as well.

TABLE 49 (continued)

Case No.	Sex	Age (Yrs)	Height (Inches)	Heart Weight (Grams)	R. ventricle measured at the conus (mm.)	Lung Weight (Grams)	Lung Examined	% of Emphysema	Type of Emphysema	Other Data
9	M	50	67	300	3	-	Left	0.5	-	Coronial autopsy because dead on arrival at hospital. Death was due to a left cerebral infarction caused by occlusion of the middle cerebral artery.
10	F	50	62	350	3	R 370 L 320	Left	0.3	A few small sub pleural cysts	Died from a traffic accident.
11	F	67	59	220	8	R 400 L -	Right	26.0	Pan acinar destructive	Admitted a few days before death complaining of chest pain, cough and dyspnoea for some time. The cough was productive with occasional haemoptysis. Examination revealed clubbing of the fingers and slightly raised J.V.P. Both lungs showed gross emphysema and there was a lobar pneumonia in the right upper lobe. The clinical signs of cor pulmonale were confirmed by the gross right ventricular hypertrophy.

The emphysema present in the 11 lowland cases over the age of 50 years was compared with that in the ser ies of 50 cases from London (Heard and Izukawa, 1964). The units of emphysema obtained in the T.P.N.G. survey were converted to the units used by the above authors for the purposes of this comparison. The two series are compared in Table 50.

TABLE 50

Lowland Cases Over 50 Years of Age Compared with a Series of Cases from London

Units of Emphysema	No. of Cases		% of Cases	
	T.P.N.G.	London	T.P.N.G.	London
None or trace	5	13	46	26
1 - 3	1	16	9	32
4 - 9	4	14	36	28
10 - 18	1	7	9	14
	11	50		

Carbon Pigmentation

The degree of carbon pigmentation was assessed by examining both the pleural surface and cut surfaces of the lungs. It was graded as mild, moderate or severe. 23 of the lowland cases exhibited mild (in many cases virtually no) carbon pigmentation (Figs. 230 & 231) and 9, a moderate degree. Of those over 50 years of age, 7 had mild pigmentation and 4 moderate pigmentation. Of the 10 lungs from the Highlands, the degree of pigmentation was noted in 9. It was mild in 8 and

moderate in 1.

The degree of carbon pigmentation observed in the lungs from T.P.N.G. was compared with that observed in the lungs from London, and this is shown in Table 51.

TABLE 51

Comparison Between the Degree of Carbon Deposition in Lungs from T.P.N.G. and London

Degree of Carbon Pigmentation	T.P.N.G. % of 41 Cases	London % of 46 Cases
Mild	74	60
Moderate	26	30
Severe	0	10

Obstructive Airways Disease Without Evidence of Emphysema

One patient in this series, a male aged 40 years, died three weeks after admission with the symptoms and signs of cor pulmonale. On admission his peak flow rate was 115 litres/min. while two days prior to death it was 60 litres/min. Post mortem examination revealed an enlarged heart (530 gms.) with gross right ventricular hypertrophy (right ventricle measured 8 mms. at the pulmonary conus). The right lung weighed 450 gms. and the left 300 gms. Both lungs showed minimal emphysema. (Fig. 232). Point counting of the left lung which was inflated and fixed showed 0.4% of the lung volume consisted of emphysema. There was marked atheroma of the pulmonary arteries, and this extended down

to the muscular arteries (Fig. 233). Patchy areas of bronchopneumonia were shown on microscopic examination.

This patient could be classified as a bronchial type of airways obstruction without evidence of emphysema, the so-called "blue-bloater". (Burrows et al. (1966)).

Bronchiectasis

In only one case examined in Port Moresby during the period of this survey was bronchiectasis found. This was in a 55 year old female who had gross bronchiectasis of the middle lobe of the right lung. The upper and lower lobes of that lung were extensively involved with acute tuberculous pneumonia. Histology revealed disseminated amyloidosis and there were heavy deposits of amyloid in the alveolar septal walls. A moderate amount of emphysema was present in this lung. Point counting of the left lung which showed no evidence of tuberculosis, revealed 9.2% of its volume to consist of emphysema. This case was omitted from the present study because of the presence of the tuberculosis.

Discussion

Prior to 1965 medical practitioners assumed that chronic non-tuberculous respiratory disease was more prevalent in the Highlands than in the lowlands. Highland people spent at least 12 out of every 24 hours inside poorly ventilated huts in which fires were kept burning throughout the night to provide warmth. On the other hand, coastal dwellers lived in houses which were better ventilated and in which fires burned for much shorter periods of time. It appeared that Highlanders were exposed to greater atmospheric pollution than were lowland dwellers.

Although the number of cases from the Highlands in this series was small, there was no indication that emphysema was more prevalent in the Highlands than in the lowlands, nor was the degree of carbon pigmentation of the lung more pronounced in the former. If anything, the reverse appeared to be true.

This observation accords well with the epidemiological investigations of Vines (1970) who measured the maximum expiratory flow performances of people living in different parts of T.P.N.G. using a Wright peak flow meter. He showed that these performances were better at high than at low altitudes, and he assumed that this was consistent with a greater prevalence of obstructive lung disease in the lowlands. He also examined the effect of domiciliary smoke upon respiratory function. He found that four of 26 people tested with the Wright peak flow meter performed as well or better in the smoky domestic atmosphere, while 22 performed worse than in the open air environment. The period of exposure to smoke had been 25 to 95 minutes. He concluded that an acute, mild obstruction of the respiratory tree occurred in the smoky domestic situation, but that it was not valid to assume from this that domiciliary smoke was the cause of chronic obstructive lung disease.

Both Vines and Woolcock and Blackburn (1967) concluded that cigarette smoking could be excluded as a cause of chronic obstructive lung disease in T.P.N.G. They suggested that repeated infection appeared to be an important factor. The latter authors were investigating the possibility that hypersensitivity to some environmental agent, for example mould in the thatch of the houses, may also be important.

The pulmonary function tests performed by Vines and by

Woolcock and Blackburn demonstrated an increasing prevalence of obstructive lung disease with advancing age in all populations studied. This was noted in both sexes and began to appear in adults over 30 years of age. The pathological studies also demonstrated an increase in the prevalence of emphysema with age, particularly after the age of 30 years. The relatively low prevalence in the 40 to 49 year age group in the present series might be attributed to the small number examined. Only 6 females were included in the present investigation; but the trend towards an increasing prevalence of emphysema after 30 years of age was nevertheless apparent.

A comparison was attempted between the prevalence and type of emphysema encountered in T.P.N.G. and in London, United Kingdom. The latter was an example of a population from a temperate climate, and a technologically advanced country. The figures from T.P.N.G. are small, and exact comparison is therefore difficult. Nevertheless it appears that the prevalence of severe emphysema - that is, those with more than 4 Heard units, or 22% of the lung volume represented by emphysema according to the Dunnill point-counting method - is no different in the two series.

In the lungs from London (Heard and Izukawa, 1964) pan acinar destructive emphysema was the commonest type encountered. This also applied to the lungs from T.P.N.G., but all the other types of emphysema described by these authors were encountered in at least one lung from T.P.N.G. The comparison between the degree of carbon pigmentation in the two collections of lungs was difficult because no really comparable objective assessment was made. Owing to the relatively small amount of carbon pigmentation in the majority of the lungs from T.P.N.G., it is probable that the author's assessment of moderate pigmentation

would have been more in keeping with the 'mild' pigmentation of Heard and Izukawa. Also, the average age of the London cases was greater than that of those from T.P.N.G. In spite of these variables however, it seems reasonable to conclude that the degree of carbon pigmentation was greater in London than in T.P.N.G., and this no doubt reflected the difference between the carbon content of the atmosphere in the two localities.

From his clinical study of 63 patients with chronic non-tuberculous lung disease attending a respiratory clinic in Port Moresby, Alpers (1968) concluded that the clinical and physiological characteristics of patients with chronic bronchitis and emphysema did not appear to differ qualitatively from similar series in other parts of the world. This pathological study confirms these observations. The clinical study began during 1967, but unfortunately none of the patients studied clinically were followed long enough for a pathological examination to be made. Such a clinico-pathological study, while being highly desirable, is extremely difficult, if not impossible, under the conditions obtaining in T.P.N.G.

Very few morphological studies of emphysema have been undertaken in people living in tropical countries. A report from Jamaica (Hayes and Summerell, 1963) indicated that the prevalence and type of emphysema occurring in the West Indies was similar to that in cities in the United States of America. In tropical countries like the West Indies and T.P.N.G. atmospheric pollution is much less than in technologically advanced countries and the existing pollution is mainly caused by smoke from domestic fires rather than by industrial waste. The fact that the prevalence and type of emphysema is similar under these two

different types of environmental conditions suggests that atmospheric pollution is not the only cause of chronic obstructive airways disease, and that some other aetiological factor may be at least as important, if not more important.

Summary

The morphological features of emphysema were studied in lungs from 42 patients on whom post mortems were performed during 1966 and 1967. There was an increasing prevalence of emphysema with age, particularly after 30 years of age. This was in agreement with epidemiological studies of respiratory function performed independently in different population groups in T.P.N.G.

The findings suggested that emphysema was more prevalent among the low land population than among the Highlanders. This, too, was in agreement with the epidemiological findings.

A comparison between this series and a similar series in London suggested that there was very little difference between the prevalence and types of emphysema in the two groups. The only marked difference was the greater degree of carbon deposition in the lungs in London.

It is suggested that atmospheric pollution was not an important cause of the emphysema occurring in T.P.N.G.

CHAPTER 16

HAEMOPOIETIC AND LYMPHORETICULAR SYSTEMS

Vines (1970) summarised the haematological data that was available from T.P.N.G. prior to 1962. This consisted mainly in reports of haemoglobin surveys in different population groups throughout the country. The differences noted in the haemoglobin values in these various groups were related to differences in altitude, hookworm infestation and malaria. Ryan (1961 & 1962), using haematological services based in Australia, demonstrated the presence of Thalassaemia and glucose-6-phosphate dehydrogenase deficiency, and pointed out that megaloblastic anaemia was an important cause of anaemia in pregnant women in the Port Moresby area. Pitney (1961) carried out a sample haematological survey during a brief visit in 1961, but no systematic haematological investigation had been undertaken by a pathologist resident in T.P.N.G.

Under the guidance of Professor W.R. Pitney, the author during 1962 attempted to establish the pattern of haematological diseases occurring in the Port Moresby area. The results of this study were presented to a meeting of the Port Moresby branch of the Medical Society of Papua-New Guinea early in 1963. In February of that year a full time haematologist was appointed to the hospital staff and the author did not engage in any further haematological investigations.

Methods

The first investigation undertaken was to establish the "normal" haemoglobin levels of the different groups of people in the

area. The haemoglobin was estimated by the oxyhaemoglobin method (Dacie, 1956) and the results were read on an EEL photoelectric colorimeter calibrated using a standard haemoglobin solution obtained from the Red Cross Blood Transfusion Service, Brisbane. All estimations except those on ante-natal patients were performed on capillary blood obtained by the finger prick technique. Approximately half the estimations were performed by the author, and the other half by an expatriate medical technologist. The ante-natal haemoglobins were performed on venous blood collected into E.D.T.A. anticoagulant. These estimations were performed in the routine laboratory under the supervision of an expatriate medical technologist. Haemoglobin estimations were performed under the same conditions on 50 Australian male blood donors to provide a standard by which to test the accuracy of the estimations.

The second part of the investigation was to determine the types of haematological diseases which were occurring in the hospital patients. In order to reduce the amount of work involved to manageable proportions, patients whose haemoglobin was 5 gms.% or less were selected for detailed study. Ante-natal patients whose haemoglobin was 9 gms.% or less were also studied in a similar fashion. The tests performed were: haemoglobin; packed cell volume; mean corpuscular haemoglobin concentration; white cell count; differential count; examination of a peripheral blood smear; and bone marrow aspiration. All patients who had a bone marrow aspiration performed were examined by the author and notes were made of any abnormal clinical findings.

Special tests performed when they seemed indicated were as follows: direct coombs test; histamine test meal; folic acid and vitamin B_{12} levels; haemoglobin electrophoresis. (These last three

tests could not be performed in Port Moresby, and blood was submitted to the laboratory of Professor W.R. Pitney for these tests.)

Biochemical tests performed on the majority of patients were: blood urea; total serum protein; paper electrophoresis of the serum proteins; serum bilirubin; serum alkaline phosphatase; serum glutamic oxalo acetic transaminase.

The response to treatment was followed in as many patients as possible by repeated haemoglobin estimations, reticulocyte counts, peripheral blood smears, and in those patients with megaloblastic anaemia, repeat bone marrow examinations. Towards the end of the year, bone marrow aspirations were performed on fewer patients with obvious iron deficiency anaemia (as indicated by the presence of a hypochromic microcytic peripheral blood film), because so few of these patients demonstrated any obvious megaloblastic change on bone marrow examination.

Results

Haemoglobin Values

The haemoglobin values of different groups of people in Port Moresby are shown in Table 52.

TABLE 52

Haemoglobin Values of Different Groups of People from Port Moresby in 1962

	Haemoglobin (grams.%)	Standard Deviation	No. Examined
Children			
3 - 5 days	17.8		40
3 - 5 years	10.9	0.98	55
6 - 10 years	11.6	1.31	103
11 - 15 years	11.6	1.66	109
Adults			
Males	13.7	2.37	145
Females	11.2	2.14	60
Ante-natal Patients	10.4	1.70	350
Medical College Recruits			
Male	14.4	1.90	74
Female	12.5	1.40	47
Teachers' College Recruits			
Male	13.8	1.64	41
Medical College Seniors			
Male	15.0	1.67	45
Female	12.8	1.40	12
Senior Soldiers	14.8	1.60	71
Australian Male Blood Donors	15.6	1.30	50

Causes of Anaemia

During the 11 month period from February 1962 to January 1963, 100 patients whose haemoglobin value was less than 5 gms.% were examined. The number of admissions from which these patients came was approximately 5,500. The causes of anaemia are listed in Table 53.

TABLE 53

Causes of Anaemia in 100 Patients Whose Haemoglobin was 5 gms.% or Less

Iron deficiency	49
Malaria	27
Cause undetermined	12
Uraemia	5
Megaloblastic Anaemia	3
Leukaemia	3
Thalassaemia	1
	100

Iron Deficiency Anaemia

This was the commonest cause of anaemia, accounting for half the cases observed. The age and sex distribution of these cases is illustrated in Table 54.

TABLE 54

Age and Sex Distribution
49 Cases of Iron Deficiency Anaemia

	Age Groups (Years)				
	0-10	11-15	16-25	26-40	40+
Males (33)	13	0	12	3	5
Females (16)	8	0	5	3	0

As can be seen from the table there were 21 children with iron deficiency anaemia and 28 adults. Of the latter, 20 were males and 8 were females. (Pregnant women were not included in this particular group. Anaemia of pregnancy was investigated separately.)

Haematological Features

All patients except two had low M.C.H.C. values and hypochromic microcytic red cells in their peripheral blood smears. No white cell abnormality was noted and platelets were normal. Two patients had normochromic normocytic red cells in their peripheral blood films and their M.C.H.C. values were in the normal range. Bone marrow aspirations on both of them showed normoblastic erythropoiesis and they both responded to oral iron therapy.

Bone marrow aspirations were performed on 22 patients. They all showed normoblastic erythropoiesis without any evidence of megaloblastic change. In all cases there was marked erythroid hyperplasia. Perl's reaction for iron was performed on seventeen of these marrow aspiration smears. They all showed gross depletion in the amount of iron present. A few granules of iron were noted in 11 cases but none

at all could be found in 6.

Clinical Conditions Present in Association with the Anaemia

The majority of patients were either complaining of symptoms of anaemia or were noted to have exceedingly pale mucosae during an attendance at the casualty section of the hospital. Clinical conditions noted in addition to the anaemia are listed in Table 55.

TABLE 55

Associated Clinical Conditions Noted Among the 49 Cases of Iron Deficiency Anaemia

Diarrhoea	5
Pneumonia	4
An obvious cause of bleeding	
Wilm's tumour	1
Gastric ulcer shown on barium meal	1
Hookworm ova in faeces	
Present	9
Absent	16
Related to child bearing	
Breast feeding a 1 year old child	1
Four children in quick succession but not pregnant at the time of admission	1
Tuberculosis	1
Congestive cardiac failure which disappeared after correction of the anaemia	1
Koilonychia	
Marked	2
Slight	2

Response to Therapy

All of these patients were treated with ferrous sulphate, two tablets three times a day, and their haemoglobins were repeated at weekly intervals. Only a few patients were given antihelminthic therapy, but the Hb. values of all of them rose. 24 patients, 4 children and 20 adults remained in hospital for 2 weeks or longer.

The response to treatment of those followed for 2, 3, 4 and 5 weeks respectively is shown in Table 56.

The average rise in Hb. value shown by each of these 4 groups of patients is indicated in the table. Overall, therapy produced a rise of approximately 1 gm.% per week. Four patients were given an intramuscular injection of Imferon after 2 weeks because they had failed to respond to oral iron. There was doubt as to whether they were actually receiving their ferrous sulphate tablets. This produced a haemoglobin rise in all four patients.

TABLE 56

Response to Treatment of 24 Patients With Iron Deficiency Anaemia

Initial Hb. (gms.%)	Weeks of Treatment					Average Rise per Week (gms.%)
	1	2	3	4	5	
2.0	-	8.2				1.8
5.0	6.4	6.4				
4.8	6.4	8.0				
2.0	3.2	5.9				
5.0	5.0	8.0				
4.6	5.2	8.0				
5.0	6.4	-	10.2			1.2
4.2	-	-	8.0			
4.2	5.9	8.9	9.0			
3.7	3.8	-	5.5			
4.2	5.5	-	6.8			
4.6	-	6.3	7.6			
5.0	4.2	-	8.9	8.0		0.9
4.6	-	7.2	-	9.3		
2.4	-	-	4.0	5.0		
3.0	2.8	2.6	-	6.3		
3.2	-	3.7	-	4.2		
5.0	4.8	4.0	7.2	9.8	10.2	1.1
4.6	-	7.6	8.0	9.3	11.4	
4.2	3.0	-	5.0	6.3	8.7	
2.0	-	3.7	5.9	6.4	8.9	
3.7	5.0	5.0	5.9	6.3	6.8	
3.7	3.8	-	5.5	-	8.5	
2.2	2.6	4.2	4.2	5.0	8.0	

Malaria

In 20 patients malarial parasites were identified in the peripheral blood film. 19 of these were Plasmodium falciparum species and the other one was Plasmodium vivax. In the remaining seven no parasites could be found. These patients had been admitted because of a febrile episode, and treated with antimalarial drugs. Blood films had been made one or two days later. These showed normochromic normocytic red blood cells together with marked polychromasia, and this was interpreted as a haemolytic anaemia due to malaria.

Cause Undetermined

Four of these patients had normochromic normocytic red cells in their peripheral blood films, and normoblastic erythroid hyperplasia in their bone marrow aspirations. They were not followed long enough to determine whether the anaemia would respond to treatment with haematinics.

Two patients had features of a haemolytic anaemia. The direct Coombs test was negative. Haemoglobin electrophoresis was performed on both patients, and this showed no abnormal haemoglobin. The cause of the haemolytic anaemia was not determined.

Two patients had features of the tropical splenomegaly syndrome (Chapter 7).

Two patients with normochromic normocytic red blood cells, and normoblastic erythropoiesis showed no response to treatment with a number of different haematinics.

One patient had cold agglutinins in such a high titre that a peripheral blood film could not be made to assess the red cell morphology. He left hospital before an adequate blood film was made.

One male child aged 4 years with tuberculosis had normochromic normocytic red cells, marked polychromasia and approximately six nucleated red blood cells per 100 white cells. Repeated blood films failed to demonstrate the presence of Malarial parasites and no explanation for this haematological picture was found.

Uraemia

All of these patients were young adults, 4 males and 1 female. Three of them were normotensive and their renal disease may have been due to amyloidosis.

Megaloblastic Anaemia

The details of these three cases were as follows:

Case 1. A female aged 27 years who was not pregnant but had delivered a child four months previously. Initial haemoglobin 4.2 gms.%; peripheral blood film showed normochromic normocytic red cells with a little polychromasia and occasional nucleated red cells. Multisegmented neutrophils were present; bone marrow showed gross megaloblastic change with numerous giant metamyelocytes. An iron stain was not performed; the Coombs test was negative; histamine-fast achlorhydria was demonstrated.

Treatment - Vitamin B_{12} injections 1,000 micrograms statim followed by 100 micrograms daily for 19 days, after which ferrous sulphate tablets

were added to the treatment.

Response to treatment

Days after treatment started	Reticulocyte Count (%)
3	14
7	14
10	50
14	90
17	11
30	6

A repeat bone marrow aspiration three weeks after commencement of therapy showed reversion to normoblastic erythropoeisis. The haemoglobin at the time of discharge one month after the commencement of treatment was 9.3 gms.%.

Case 2. A male aged 25 years working as a labourer complained of giddiness and headache and fell down while working. His employer sent him to the hospital for investigation. His haemoglobin was 3.3 gms.%, the peripheral blood film showed normochromic normocytic red cells and a slight polychromasia. The bone marrow aspiration showed gross megaloblastic erythropoiesis with occasional giant metamyelocytes. Iron was grossly reduced. Free acid was present in the gastric juice.
Treatment - folic acid tablets 30 mgms. daily.
A marked reticulocytosis occurred with a maximum count of 14% on the twelfth and fourteenth days with a fall during the subsequent week. The haemoglobin rose steadily, and was 9 gms.% at the time of discharge one month after commencement of therapy.

Case 3. A male aged 50 years was admitted because he felt

vaguely unwell. His haemoglobin was 2 gms.%, the red cells were normochromic normocytic and a few macrocytes were noted. The bone marrow showed marked megaloblastic erythropoiesis with numerous giant metamyelocytes. The iron was grossly reduced. Free acid was present in the gastric juice. A Vitamin B_{12} assay showed normal levels and the folic acid was 1.4 milli micrograms/ml.

Treatment - folic acid tablets 30 mgms. daily.

Response to treatment

Days after treatment started	Reticulocyte Count (%)
1	2
7	10
14	10
20	4

The haemoglobin rose to 6,8 grams % one month after admission, and a repeat bone marrow aspiration showed reversion to normoblastic erythropoiesis.

Leukaemia

The details of the three patients were as follows:

Case 1. A male aged 16 years was admitted for investigation of bleeding gums. Liver and spleen were not palpable. There was no lymphadenopathy and no bone tenderness. The peripheral blood and bone marrow examination revealed the presence of an acute myeloblastic leukaemia. He was treated with blood transfusions, 6 mercaptopurine and cortisone. He was discharged, but died three months later.

Case 2. A female aged 2½ years was admitted for investigation

of a mild upper respiratory tract infection and lassitude. Liver and spleen were not palpable, and there was no lymphadenopathy. The peripheral blood and bone marrow examination revealed an acute lymphoblastic leukaemia. She died one month after admission.

Case 3. A male aged 32 years was admitted for surgical treatment of haemorrhoids. Liver and spleen were not palpable. There was no lymphadenopathy, no sternal tenderness, and no other clinical abnormality. Examination of the peripheral blood and bone marrow showed an acute lymphoblastic leukaemia. He died one month after admission.

During this period five other patients were diagnosed as suffering from leukaemia. Two of these, both males, one aged 42 and the other aged 30 years, had chronic myeloid leukaemia. Two males, one 20 years and the other 60 years of age had acute lymphoblastic leukaemia. The fifth patient was a male student aged 20 years who had chronic lymphocytic leukaemia. He was admitted for treatment of a tropical ulcer on his leg, and the diagnosis of leukaemia was made when a routine peripheral blood film was examined. He had gross splenomegaly which he was sure had been present for the preivous five years. X-ray therapy to his spleen caused reduction in its size, and his white cell count fell from 150,000 per cubic m.m. to 76,000 per cubic m.m. He was discharged and lost to follow-up.

Thalassaemia

The only new case of Thalassaemia diagnosed during the 11 month period was a five month's old girl who had Thalassaemia major. Her brother had died some months previously and had been shown to have Thalassaemia major. Haemoglobin electrophoresis revealed that virtually

all the haemoglobin was HbF. Radiological examinations revealed none of the bone changes sometimes seen in patients with Thalassaemia. Haematological investigation of the father showed no abnormality. The mother had a haemoglobin of 9.6 gms.% and an abnormally high level of HbA_2.

Discussion

Anaemia has been recognised for many years as a major medical problem among the indigenous inhabitants of tropical countries. Investigations into the causes of these anaemias have been difficult for a number of reasons. Firstly, the cause of any anaemia is usually multifactorial. Dietary deficiency of multiple haemopoietic factors, malaria and other parasitic infestations are almost invariably involved. Secondly, laboratory facilities are usually limited, and to investigate these anaemias properly a large amount of sophisticated equipment and a number of highly skilled laboratory workers are required. Thirdly, long-term hospitalisation and follow-up is necessary for thorough investigation, and patients who live at some distance from the hospital are unwilling to stay away from their homes and families for extended periods of time.

The present investigations showed that iron deficiency anaemia was the commonest type. Nearly half of these patients were children. If young adult pregnant women had been included, iron deficiency anaemia would have been seen to occur most frequently in children and in pregnant women.

Anaemia due to malaria was next in frequency. Megaloblastic

anaemia was important particularly in pregnant women. Anaemia due to haemoglobinopathies and to gross splenomegaly were also important. As indicated by Pitney (1971) in a recent review entitled "Anaemia in the Tropics" the pattern of anaemia found in Port Moresby was fairly typical of that found in most other tropical countries throughout the world.

The author demonstrated that haemoglobin values changed progressively with age. Vines (1970) noted a similar progressive change in haemoglobin value with age. He compared this with the Australian population. The overall pattern was similar, but the actual levels of haemoglobin were lower in T.P.N.G. The values obtained for children and adults in the present investigations were 1 to 2 grams higher than those recorded by Vines in his coastal population group. They agreed more closely with the values obtained for children and adults living in the urban area of Rabaul (Kariks, 1969). The mean haemoglobin of pregnant women was similar in all three investigations. Vines was investigating people living under village conditions, while Kariks and the author were investigating urban populations. This may account for the differences in the haemoglobin levels.

In the present investigations the haemoglobin values of students (both males and females) at the time of recruitment for tertiary education were higher than the values observed in the local population. The haemoglobin values of male medical college students and soldiers from the Pacific Islands Regiment three or more years after recruitment, showed even higher levels of haemoglobin. These were approaching the haemoglobin values of Australian male blood donors living in Port Moresby. These Papuans and New Guineans had been attending boarding schools for many years, and their diets had been supervised.

They had been taking drugs to suppress malaria and had been under constant health surveillance. The progressive rise in haemoglobin value was less marked in female students, but even so their haemoglobin levels were above those of the local inhabitants of Port Moresby. These results indicate that the level of haemoglobin is more dependent on environmental than on genetic factors.

Iron deficiency was the most common form of anaemia encountered. This was due to bleeding in two cases and was related to pregnancy and child birth in another two. Hookworm ova were found in the faeces of only 9 of the 25 patients examined. This was probably inaccurate because hookworm infestation was very common. Ova were present in between 70 and 90 per cent of the different groups of people examined by Vines (1970). At the time of this investigation specimens of faeces were difficult to obtain from patients, and the technician examining them for ova was inexperienced. The part played by the hookworms in the causation of the iron deficiency anaemia was therefore not ascertained.

The other conditions which occurred in association with the anaemia namely, diarrhoea, pneumonia and tuberculosis, were not necessarily associated with it. The only epithelial change noted was koilonychia.

Only small amounts of iron were found in bone marrow aspirates. Perl's stains performed on livers obtained at post mortem also revealed only small amounts of iron. These observations indicated that the iron present in the body stores was depleted. This is a common finding in many tropical countries. (Pitney, 1971).

Only 24 patients remained under observation for long enough for their response to treatment to be assessed. All of them showed a good response to treatment with oral iron preparations in spite of the fact that anti-helminthic therapy was given to only a small number of them. No comparable study has been reported from T.P.N.G., but Pitney (1971) refers to similar findings in other tropical countries.

Malaria was frequently encountered in hospital patients and it was an important cause of anaemia.

The patients grouped under the heading "Cause undetermined" formed a heterogeneous group. The four patients with normochromic normocytic red cells may have had a mixed type of anaemia with iron and folic acid deficiency. Two patients were probably suffering from the tropical splenomegaly syndrome which is referred to in Chapter 7, while two others had haemolytic anaemia, the cause of which was not ascertained. Cold agglutinins were frequently encountered (Booth, 1965) but their significance has not yet been determined.

Five of these anaemic patients were suffering from chronic renal disease. This is discussed further in Chapters 2 and 3.

Only three patients with megaloblastic anaemia were encountered. During the subsequent six years the relative rarity of megaloblastic anaemia in non-pregnant patients in the Port Moresby area was confirmed. (Booth, 1967). It was interesting that two of the patients in the present series were males and neither of these had steatorrhoea. Booth also encountered two males with this form of anaemia. No specific cause could be found in one, while the other had haemoglobin H disease. In addition to this, five of the sixteen patients with megaloblastic

anaemia reported by Powell and Booth (1969) were males, and none of them had any evidence of malabsorption. The occurrence of megaloblastic anaemia in males in T.P.N.G. seems to warrant further investigation. It is likely that these patients were suffering from "tropical sprue", but this diagnosis was not confirmed. Tropical sprue occurred in a number of expatriate residents of Port Moresby (personal observation), but no case was diagnosed in the indigenous people.

The female patient with megaloblastic anaemia in the author's series may possibly have had vitamin B_{12} deficiency because of the histamine-fast achlorhydria. This could not be proven however, in the absence of more sophisticated tests. The therapeutic response to treatment with vitamin B_{12} was impressive, but the dose was too large for this to be used as an argument in favour of the diagnosis of pernicious anaemia. No case of proven pernicious anaemia occurred up to the end of 1967. (Booth, 1967).

Unfortunately the data relating to the investigation of the 100 ante-natal patients whose haemoglobin was less than 9gms.% has been lost. Iron deficiency was the commonest cause of anaemia. The other conditions noted in the present investigation were also encountered in pregnant women, but approximately 10 of the patients had marked megaloblastic anaemia. The impression gained from the report by Ryan (1962) was that megaloblastic anaemia of pregnancy was extremely common. This was not borne out by the author's experience nor by that of Booth (1967) who reported 21 cases of folic acid deficient megaloblastic anaemia of pregnancy over a 2½ year period. Thus, while it was a very important cause of anaemia of pregnancy, it was not as common as was previously suspected.

Only eight cases of leukaemia were recorded from all parts of T.P.N.G. from 1958 to 1961. The author diagnosed eight cases in the Port Moresby hospital alone during 1962. This indicated that leukaemia had previously been grossly under-diagnosed. This was further emphasised by Booth (1970) who reported 97 cases of leukaemia diagnosed throughout T.P.N.G. between 1958 and 1967. During 1967 alone there were 23 cases referred from all parts of the country. She confirmed that as in Africa, malignant lymphoma was much more common in children than was acute leukaemia. A number of patients with acute myeloid leukaemia were diagnosed by the author from biopsies taken from subcutaneous "tumours". In Africa, chloromas occur relatively frequently. (Davies and Owor, 1965). Booth (1970) did not have enough cases to comment on the prevalence of chloroma in T.P.N.G.

Only one new case of Thalassaemia was diagnosed. This was in agreement with the experience both before 1962 and since then, that Thalassaemia was relatively rare.

As was mentioned in Chapter 2, multiple myeloma appeared to be a rare disease, only one case being diagnosed between 1962 and 1967.

Summary

A study was made of the normal haemoglobin values and of the haematological conditions occurring in the Port Moresby area during 1962. The pattern found resembled that in many other tropical countries.

Iron deficiency was the commonest cause of anaemia. Children and pregnant women in particular were affected. It was shown that the anaemia would respond to treatment with oral iron supplements if such

treatment could be continued for a number of weeks.

Malaria was the second most common cause of anaemia.

In one group of anaemic patients no satisfactory cause was found. Two of these patients had the syndrome described as tropical splenomegaly, and five were uraemic.

Megaloblastic anaemia accounted for only a small number of patients in this survey, but it was an important cause of anaemia in pregnant women. Attention was drawn to the occurrence of megaloblastic anaemia in males. No satisfactory explanation for this was found, but these patients may have been suffering from tropical sprue.

Leukaemia was under-diagnosed prior to 1962. Even by 1967 it was probably still under-diagnosed. However, malignant lymphoma was more prevalent in children than was leukaemia. This phenomenon resembled the situation in Africa. Another similarity to the African situation was the relative frequency with which chloromatous deposits were found in patients with acute myeloid leukaemia.

Haemoglobinopathies and multiple myeloma did occur, but they were relatively rare.

Spleen

Splenomegaly was a very common physical finding in T.P.N.G. because of the widespread occurrence of malaria. The size of the spleen rendered it liable to traumatic rupture - for example, in traffic accidents; as a football injury; following a blow to the abdomen with a blunt instrument; and in one relatively minor aircraft crash, a passenger

with splenomegaly ruptured his spleen as he was thrown against his lap type seat belt at the time of impact. The very large spleens seen at post mortem were usually freely mobile and only occasionally were adhesions present between the capsule and the parietal peritoneum. Malarial pigment was commonly found in histiocytes lining the sinusoids of the white pulp, and miliary tubercles were often seen in cases of miliary tuberculosis.

Pitney et al, 1968 examined 15 spleens removed surgically as treatment of tropical splenomegaly. (see Chapter 7). These spleens ranged in weight from 2,090 to 4,380 gms. Large histiocytes, often containing ingested red cells, were seen in imprint smears from the cut surfaces of the spleens. Histologically, dilated splenic sinusoids appeared to be a uniform finding in all of them.

Lymph Nodes

Normal Features

Small amounts of melanin pigment were frequently found in otherwise normal lymph nodes. Inguinal lymphadenopathy was very common, and palpable nodes were often biopsied at the time of surgical biopsy or excision of squamous carcinomas of the lower leg. The nodes which contained no secondary tumour were enlarged and rubbery. Their normal architecture was distorted and there were islands of lymphoid tissue separated by bands of fibrous tissue. These changes were presumably due to the effects of chronic inflammation resulting from repeated abrasions to unprotected legs and feet.

Inflammatory Conditions

The commonest of these were tuberculosis and filariasis. These were dealt with in Chapter 9.

Malignant Lymphoma

Malignant lymphomas (excluding Burkitt's lymphoma which was discussed in Chapter 5) accounted for 7% of all the malignant neoplasms notified to the tumour registry. They were the third most commonly reported tumour. Booth et al (1969) reviewed 157 of these neoplasms. Their findings were as follows.

The clinical features and the histological appearances were similar to those found in other countries. All the well recognised types of malignant lymphoma occurred with the exception of giant follicular lymphoma. A greater proportion of the cases from T.P.N.G. occurred in children than is found in countries such as Australia. This was probably due to the different age structure of the population. The difference in age structure may also account for the absence of cases of giant follicular lymphoma.

The male to female ratio of cases was 3:2 which probably meant that there was no difference in prevalence between the sexes.

Cases were diagnosed in all parts of T.P.N.G. There was no clustering of cases in any particular region.

CHAPTER 17

NEONATAL & FORENSIC PATHOLOGY

Neonatal Pathology

During the four years 1962-3 and 1966-7 the author reported on the histological sections from 81 neonatal autopsies (i.e. infants up to one month of age). The causes of death are listed in Table 57.

TABLE 57

Causes of death in 81 Neonatal Autopsies

Pneumonia		37
	Non specific 34	
	Giant cell 2	
	Tuberculous 1	
Prematurity		13
No cause determined		8
Massive pulmonary haemorrhage (2 of these were identical twins whose death occurred 2 days apart)		5
Meningitis		3
Haemorrhage from tears of tentorium cerebelli		2
Intracerebral haemorrhage - no specific cause found		1
Myocarditis - no specific aetiology found		1
Cytomegalovirus infection involving kidneys, liver and lung with hydrocephalus and calcification of ependymal lining of lateral ventricles		1

TABLE 57 (continued)

Congenital abnormalities	
Hydrocephalus	2
(one with Arnold Chiari malformation and meningomyelocoele)	
Congenital heart disease of various types	4
Exomphalos	1
Multiple atresias of small intestine	1
Imperforate anus	2
(Both had congenital heart lesions, and horseshoe kidneys, and both died of pneumonia)	
	81

This range of pathological findings could occur in a review of almost any series of neonatal autopsies, and nothing specifically relating to T.P.N.G. emerged. The autopsies were performed in a rather haphazard fashion in that they were done only when the Obstetrician or the Paediatrician decided to ask for an autopsy, and when the parents consented to this.

No attempt at a formal neonatal mortality survey was made. Indeed this would have been very difficult because the size and composition of the population in any particular locality was not known with certainty; only a minority of babies were being born in hospital; and permission for autopsies was often difficult to obtain.

This review concerned neonatal deaths mainly from the vicinity

of Port Moresby. However, it may be useful as a guide to more detailed neonatal mortality surveys which may be conducted at some future date.

Forensic Pathology

Forensic pathology formed a significant component of the work of the pathologist in Port Moresby. Prior to 1962 this work had been done by whatever medical officer could be spared from clinical duties to do it. These doctors had no special interest or training in this field and the records were of variable quality. During the 1960's the legal system was becoming more sophisticated, and there was a growing demand for a greater amount, and a higher standard of forensic pathology throughout T.P.N.G. The following is an account of the first systematic study of a series of autopsies on people dying from unnatural causes.

Material

166 forensic autopsies on indigines in Port Moresby between 1962 and 1967 were selected for study. The majority of these were performed personally, most of those in 1964-65 having been excluded. Also excluded were autopsies on expatriates and on the victims of fatal aircraft accidents.

Results

The autopsies were divided into three groups - Accidental deaths, Suicide and Homicide. The causes of the first group are listed in Table 58.

TABLE 58

Accidental Deaths

Traffic accidents	42
Industrial accidents	13
Drownings	20
Ruptured spleen	8
Cerebral haemorrhage from head injury	5
Inhaled foreign body	4
Miscellaneous single causes	16
	108

Traffic Accidents

Post mortems were not performed on all casualties from motor traffic accidents owing to the increasing rate at which they occurred during 1966-67. A wide variety of trauma was seen in these post mortems; but if there was abdominal injury, it was unusual not to find a ruptured spleen, either alone or in association with rupture of other viscera.

Industrial Accidents

The types of accidents reflected the various types of work available for unskilled labourers. Six men were killed by crush injuries to the abdomen caused by machines such as tractors, a bulldozer and a front-end loader. These injuries caused rupture of abdominal viscera including the spleen in 5 cases. Two men died on rubber plantations from head injuries caused by falling rubber trees. Two died of

electrocution; two died of traumatic asphyxia when the lower halves of their bodies were trapped by a fall of earth when the sides of a trench caved in; and one dairy worker died from the effects of a ruptured spleen after being kicked by a cow.

Drownings

There were 20 drownings. Port Moresby was situated on the coast and the village houses were characteristically built over the sea. However, only 3 of the drownings were of young children from coastal villages. The remainder were adults, almost exclusively labourers recruited from the Highlands. These young men worked on plantations in the hinterland of Port Moresby. They had no previous swimming experience, and invariably the story was that they had jumped into a river or a dam in the manner of the local Papuans.

Ruptured Spleen

These 8 cases (6 adults and 2 children) sustained abdominal injury either while playing games, particularly football, or as a result of falling from trees.

Cerebral Haemorrhage from Head Injury

All 5 of the haemorrhages were associated with a fractured skull. Three were subdural. Two of these casualties were dead on arrival at hospital and the cause was not found. The third was a patient who fell out of bed onto the concrete floor of the ward.

One extradural haemorrhage was sustained by a child who fell

while at play. The fifth case was a subarachnoid haemorrhage. The cause of the injury was not ascertained.

Inhaled Foreign Body

In all 4 of these cases (2 adults and 2 children) the foreign body was a large bolus of food, which had lodged either in the larynx or in the trachea. In all of them, the stomach was filled with recently ingested food.

Suicide

There were 16 suicidal deaths. The methods used were as shown in Table 59.

TABLE 59

Suicidal Deaths

Hanging	10
Shooting	3
Stabbing	1
Poisoning (lovers)	2
	16

Of the sixteen, thirteen were males and three were females. The majority were young adults. Most were non-permanent residents of the Port Moresby area. The hanging was usually done inside a dwelling. The "rope" consisted of a short cord, or cloth rolled into a cord,

twisted around the neck and hooked on to some projection at head height or just above it. The actual hanging was accomplished by bending the knees and pulling the noose taught.

The two suicides by poisoning were accomplished by eating derris roots. No specific features were noted in these two post mortems.

Homicide

The 42 homicidal deaths were inflicted as shown in Table 60.

TABLE 60

Homicidal Deaths

Stabbing	20
Axe wounds	7
Trauma from blunt instruments	5
Spears	3
Fist fighting	3
Shooting	4
	42

Almost all the stabbings were with knives. Other instruments used included a pick axe and a small gouge used for extracting sap from rubber trees.

The exact site of the stab wounds was not recorded for seven cases in the synoptic records available to the author at the time of this writing. The chest and upper abdomen were the sites of the wounds

in nine cases. Three of these wounds were inflicted from behind. Other sites involved in single cases were: the head (with penetration of the knife to sever both cerebral peduncles), the neck, the popliteal artery and the femoral artery.

All the axe wounds were inflicted with steel axes and the wounds were mainly in the region of the head and neck.

The murder weapon was identified in only a few cases when the trauma was inflicted with blunt instruments. In one, a length of metal pipe was used, while in another, a large stone was dropped on the victim's head while he was sleeping. The cause of death in these cases was either cerebral haemorrhage associated with skull fractures or haemorrhage from a ruptured spleen.

The three deaths from fist fighting were due to cerebral haemorrhage - two subdural and one pontine. None of these was associated with a fractured skull.

Discussion

As far as could be ascertained, the pattern of deaths from unnatural causes in other centres in T.P.N.G. was similar to that seen in Port Moresby, except that in more primitive areas there were no deaths from "Industrial accidents". In these areas this group of accidental deaths was replaced by deaths caused by falling from trees, rolling into domestic fires burning inside the houses, and injuries received from encounters with animals.

Motor vehicles, particularly small trucks, were being bought by village groups and by individuals in increasing numbers from 1965.

Generally speaking these vehicles were not well maintained and were often driven by careless drivers who, particularly on the weekend following each fortnightly pay-day, were liable to be drunk. In addition to this, the roads were often in a poor state of repair and the trucks were always crowded. These conditions now obtain in most towns in T.P.N.G., and an increase in the numbers of deaths from traffic accidents can, unfortunately, be confidently predicted.

Deaths from industrial accidents all occurred in men brought up in a primitive agricultural environment. At the time of death they were working in surroundings and with implements which were foreign to their own cultural backgrounds.

In all the accidental deaths splenic rupture was a constantly recurring feature. A few homicidal deaths were also due to splenic rupture following abdominal trauma caused by a blow with a blunt instrument. Malaria was endemic in most parts of the country and as a result of this, splenomegaly was common. Traumatic rupture is one of the well-known complications of splenomegaly.

The deaths due to inhaled food particles may have been due partly to the fact that much of the food eaten by the people was rather "chunky" - sweet potato, coconut, pumpkin, tropical fruits and rice prepared to a sticky, semi-solid consistency; and partly due to a lack of readily available first aid and medical treatment.

Suicide was relatively uncommon among the people of T.P.N.G. (approximately 0.7 per 100,000) (Parker and Burton-Bradley, 1966). Determining the motives for the suicidal attempts was difficult, partly because of the language barrier, and partly because most of the histories

had to be inferred from information obtained by questioning relatives. It was thought that depression was an uncommon ingredient in the motivation. A sense of shame for inadequate performance in some aspect of life, or for some transgression of behavioural codes was commonly present. This sense of shame was probably the dominant motivating factor. The people usually attributed deaths which were not due to old age or to obvious trauma, to sorcery or poisoning. Mostly a demonstrable pathological cause could be found, but poisons were well known, and true poisoning deaths were recorded both in Port Moresby and in other centres.

Intertribal warfare was rife before the establishment of the Australian Administration. Disputes over land, pigs, fishing grounds or women were typically settled in this way. As was revealed in the murder trials, most of the homicides were committed as a result of disputes over similar things. Women were regarded as inferior beings, and a number of these homicides involved wife murder for relatively trivial offences.

When a member of one clan was killed, there was a solemn obligation on the relatives to kill a member of the opposing clan. This philosophy is still widely held, and "pay-back" killings are the order of the day.

Most of the homicides involved single deaths, but on two occasions during the present review there were multiple deaths (and many severe injuries) following fights between different clans brought together as a work force on plantations or big construction jobs. The weapons used were similar to those used in the intertribal fights,

namely clubs, axes, spears, bows and arrows. The four shootings were all with shot guns which had been purchased primarily for hunting game.

Summary

A brief account has been given of some personal experience in the field of Forensic Pathology in T.P.N.G. The causes of unnatural death - accidents, suicide and homicide - reflected the social and cultural conditions prevailing at the time.

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